DISSERTATION ON

PREVALENCE OF METABOLIC SYNDROME IN CAD AND CVA PATIENTS AT THANJAVUR MEDICAL COLLEGE

SUBMITTED FOR

M.D. BRANCH - I

(GENERAL MEDICINE)

THANJAVUR MEDICAL COLLEGE

THANJAVUR

THE TAMILNADU DR.MGR MEDICAL UNIVERSITY

FOR THE EXAMINATION IN MARCH 2009.

CERTIFICATE

This is to certify that dissertation entitled **'Prevalence of Metabolic syndrome in CAD and CVA patients at Thanjavur Medical College'** is the bonafide record of work done by **Dr.S.SANGEETHAMEENA** in the Department of General Medicine, Thanjavur Medical College, Thanjavur during her Post Graduate Course from 2006-2009. This is submitted as partial fulfillment for the requirement of M.D Degree Examinations - Branch I (General Medicine) to be held in March 2009.

Professor and Head,
Department of General Medicine,
Thanjavur Medical College,
Thanjavur.

Unit Chief
Department of General Medicine,
Thanjavur Medical College,
Thanjavur.

The Dean
Thanjavur Medical College,
Thanjavur.

ACKNOWLEDGEMENT

I extend my thanks to the Dean Dr.P.Jayanthi MD., and our former Deans Dr.R.M.Natarajan M.S., Dr.S.Balakrishnan M.D., for having granted me permission to do this dissertation in Thanjavur Medical College, Thanjavur.

I extend my sincere and heartfelt thanks to our professor and Head of the Department of Internal Medicine Prof.Dr.S.Muthukumaran M.D., He has been a source of inspiration in conducting this study. Without his guidance this study would not have been possible.

I am very grateful to my unit chief and teacher Dr.D.Swaminathan, M.D who taught me the essentials of clinical medicine, knowledge of which is a prerequisite for pursuing dissertation of any sort and for guiding me in every step of this dissertation.

I am thankful to my former unit Assistant Professors Dr.K.Nagarajan M.D., and Dr.C.Paranthagan, M.D., for their invaluable suggestions and support. I do extend my thanks to my present Assistant Professors Dr.V.P.Kannan MD., and Dr.E.Bobby MD., who have been of great help in conducting this study.

I am grateful to all other unit chiefs of the Department of Medicine for having permitted me to work on their patients in their respective wards. With earnest sincerity, I thank the professor of cardiology Dr.K.Meenakshi M.D., D.M., Assistant Professors Dr. G.Senthilkumar M.D., D.M., Dr.G.Marimuthu M.D., D.M., Professor of Neurology Dr.P.S.Ganesan M.D., D.M., Assistant Professors Dr.M.Anguraj M.D.,

D.M., and Dr.M.Thangaraj M.D., D.M., for the support they extended for conducting this study.

I also extend my thanks to the Biochemistry department and Lab Technicians who gave me a great support in bringing out this study.

I am happy to acknowledge the role played by my patients in conducting this study without whom this study would not have been possible.

I dedicate my study to my family members who gave me love, care, comfort and to my friends and colleagues who supported me in all aspects.

PREVALENCE OF METABOLIC SYNDROME IN CAD & CVA PATIENTS AT THANJAVUR MEDICAL COLLEGE HOSPITAL.

INTRODUCTON :

The recognition of the existence of metabolic syndrome (MetS) has developed over the last two decades, following the description of an insulin resistance syndrome or syndrome X in 1988.

Depending on the definition used, the metabolic syndrome may include measures of general obesity (as reflected by BMI), central obesity (as reflected by WC or WHR), dyslipidemia (low HDL-C and / or high Triglyceride levels), hyperglycemia, high blood pressure and resistance to the action of Insulin. *(Reaven, 1988; Kaplan, 1989; Byre and wild, 2000) [56].

The increasing prevalence of obesity across the world will result in increasing prevalence of metabolic syndrome.

The increasing prevalence of metabolic syndrome increases the risk for developing diabetes and cardiovascular disease.

This study was conducted in hundred patients who presented with either CAD or CVA to know the prevalence of metabolic syndrome and its individual components as per NCEP: ATP III 2001 criteria.

AIMS OF THE STUDY :

1. To asses the prevalence of metabolic syndrome in CAD patients.

2. To assess the prevalence of metabolic syndrome in CVA patients.

3. To study the association of central obesity, Dyslipidemia Hypertension, Diabetes, smoking and alcohol with metabolic syndrome.

4. To study the difference in distribution of Metabolic syndrome in young and old.

5. To study the difference in distribution of metabolic syndrome in males and females.

HISTORY :

The term 'Metabolic Syndrome" dates back to atleast the late 1950s, but came into common usage in the late 1970s [22].

The clustering of cardiometabolic risk factors was first pointed out by KYLIN more than eight decades ago.

1947- The Marseilles physician Dr.Jean Vague made the interesting observation that upper body obesity appeared to predispose to diabetes, atherosclerosis, gout and calculi.

1977- Haller used the term "Metabolic syndrome" for associations of obesity, Diabetes mellitus, hyperlipoproteinemia, hyperuricemia & Steatohepatitis .

1988- GERALD M. REAVON in his famous Banting lecture proposed insulin resistance as the underlying factor and named the constellation of abnormalities 'Syndrome x'.

DEFINITION :-

The clustering of Insulin resistance, dysglycemia, dyslipidemia and hypertension was originally defined as Syndrome X in 1988 by Reaven. WHO, EGIR, NCEP - ATP III have added measurement of central obesity in the definition of metabolic syndrome between 1999 & 2000. Latest world wide definition is given by IDF. (Ecker et al;) [12].

OTHER NAMES OF METABOLIC SYNDROME :

Syndrome X, Insulin Resistance Syndrome, Reaven syndrome, Cardio metabolic syndrome, Deadly quartet [10].

PREVALENCE OF METABOLIC SYNDROME :

GLOBAL SCENARIO :

The current global prevalence of metabolic syndrome is approximately 16 %. [63]

In United states, as per ATP III Criteria the unadjusted and age adjusted prevalence of metabolic syndrome, were 21.8% and 23.7% respectively.

Prevalence increased from 6.7% among participants aged 20-29 years to 43.5 % and 42 % for participants aged 60-69 yrs and aged at least 70 years respectively (JAMA 2002; 287: 356-359).

Age adjusted prevalence was similar for men (24%) and women (23.4%). However, African American (57%) and Mexican American (26%) Women had higher prevalence than men.

INDIAN SCENARIO :

Among Urban Indians, age adjusted prevalence was 22.9% in men and 30.9 % in Women (R. Gupta et al ;) [51]

Chennai Urban Rural Epidemiology study (CURES) estimated the prevalence in Urban south Indian Population to be 23.2% by WHO criteria, 18.3% by ATP III criteria and 25.8% by IDF criteria. (Dr.V.Mohan et al;) [9]

FACTORS THAT INFLUENCE METABOLIC SYNDROME [29] :

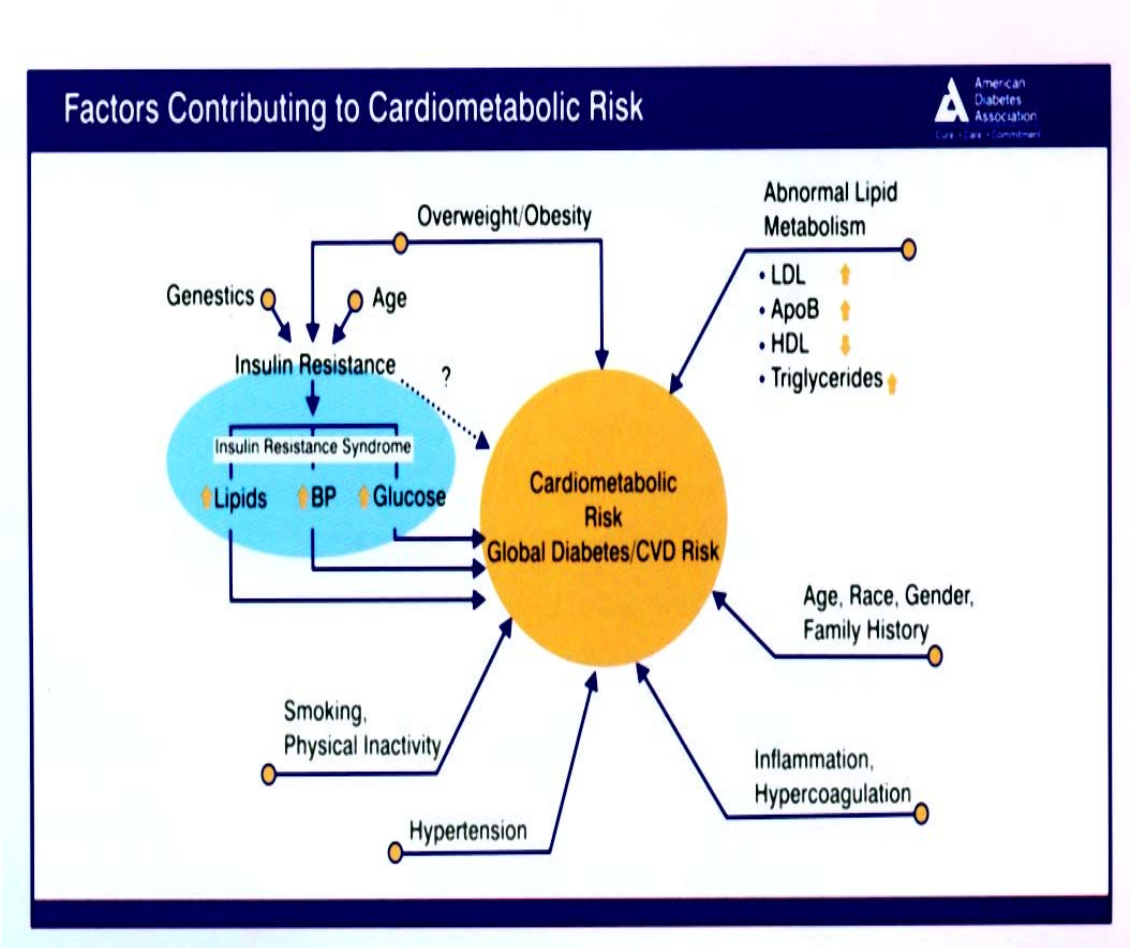


Fig 1.1

The term "Cardiometabolic risk' describes a set of risk factors, that when viewed together, are good indicators of a persons overall risk of developing heart disease and Type 2 Diabetes.

1. OVERWEIGHT / OBESITY :

Central adiposity is a key feature of the syndrome. However patients with normal weight may also be insulin resistant and have the syndrome. (Ho et al; 2001) [24].

2. DIET :

IR is inversely associated with whole grain food, dietary fibres, cereal and fruit fibers. It is positively associated with glycaemic index, glycaemic load and saturated fat intake. (Framingham offpring study, MCKeown et al; 2004) [42].

3. SEDENTARY LIFE STYLE :

Physical inactivity is a predictor of cardiovascular disease and related mortality in association with other metabolic risk factors [60].

4. AGE :

Prevalence of most individual risk factors within metabolic syndrome increases with age, at least to late middle - age and prevalence of MetS is associated with age in the same way [65].

Data on prevalence of metabolic syndrome in Children are limited but high prevalence has been reported among obese Children of 9-12 yrs old in Hong Kong (Sung et al ., 2003) [61] and in USA (weiss et al., 2004) [68].

5. GENDER :

MetS is generally prevalent in females higher than males. (onat et al., 2002) [48]. It is mainly observed in Indian, Iranian and Turkish Populations.

Increase in waist circumference predominate in women whereas fasting Triglyelrides > 150mg / dl and hypertension are more likely in men.

6. ETHNICITY :

Generally, there is higher prevalence of metabolic syndrome in Non-European groups. South Asians, Black African, Caribeans, Hispanics and significantly lower prevalence in European white and chinese, (Mckeigue, P.M.1992) [40,41].

7. BIRTH WEIGHT :

Low Birth weight is associated with higher prevalence of metabolic syndrome in Adult life. (Yarbrough etal., 1998) [69].

8. GENETIC FACTORS :

Certain components of MetS may be influenced more strongly by environment and others by genetic inheritance [52].

Eg : Environmental factors were more important for WHR, Fasting Insulin and Triglycerides.

Genetic influences were for glucose intolerance, overall obesity and low HDL - C. (Poulsen et al., 2001) [50].

9. ENDOCRINE FACTORS :

Hyperandrogenemia, PCOS, low total testosterone and SHBG levels, GH-IGF axis, glucocorticoid excess - all these predict the development of metabolic syndrome and Diabetes. (Laaksonen et al., 2004) [33].

10. MENOPAUSE / HRT :

Menopause is associated with increased amounts of abdominal visceral fat independent of aging.

Research is required to clarify the relationship between HRT use and prevalence of MetS, as there are discrepancies. (Poehlman and Tchernof, 1998) [49].

11. INFLAMMATION :

Chronic subclinical inflammation is associated with insulin resistance and metabolic syndrome[47].

12. ALCOHOL :

Alcohol consumption is associated with ↑ HDL, ↑TGL, ↑BP and therefore, has different effects on different aspects of MetS.

13. CO - MORBIDITY :

In people with Diabetes mellitus, Hypertension, CHD, prevalence of metabolic syndrome is considerably higher[54].

Among people with mental illness, notably schizophrenia prevalence of MetS was higher.

Use of ART in HIV patients is associated with increased risk of MetS.

14. LIPODYSTROPHY :

Both acquired and genetic causes of Lipodystrophy predispose to severe Insulin Resistance and hence to metabolic syndrome.

INSULIN RESISTANCE :

Insulin resistance is a syndrome characterised by a diminished ability of insulin to perform its normal physiological functions. IR is the main feature of Type 2 Diabetes and a key factor in the development of metabolic syndrome [16].

ABNORMALITIES ASSOCIATED WITH IR :

1. Glucose Intolerance:

   - Impaired fasting glucose

   - Impaired glucose tolerance

2. Abnormal Uric Acid Metabolism.

   ↑ Plasma Uric Acid Concentration

   ↓ Renal Uric Acid clearance

3. Dyslipidemia :

   ↑ Triglycerides, ↓ HDL-C, ↓ LDL - Particle diameter,

   ↑ Postprandial lipaemia.

4. Hemodynamic :

   ↑ Sympathetic Nervous System activity

   ↑ Renal sodium retention

   ↑ BP (50% patients with hypertension are IR)

5. Haemostatic

↑ PAI - I, ↑ Fibrinogen

6. Endothelial Dysfunction

↑ Mononuclear cell adhesion

↑ Plasma concentration of asymmetric diethyl arginine

↓ endothelial dependant vasodilatation

↑ Plasma concentration of cellular adhesion molecules.

7. Reproductive :

PCOS

Homeostatic Model Assessment (HOMA) [39] equation for IR.

$$\text{Insulin Resistance} = \frac{\text{Glucose x Insulin}}{405}$$

Glucose in mgldl and se. Insulin in μU / ml

If glucose is in mmol / L, divide by 22.5.

PATHOGENSIS OF METABOLIC SYNDROME :

Sedantary lifestyle and high dietary caloric intake leads to decreased free fatty acid and glucose oxidation leading on to body fat accumulation and resistance to biological action of Insulin.

Increasing levels of obesity leads to increased secretion of proinflammatory cytokines like TNF ά, IL-6, IL-Iβ from adipose tissue. These cytokines leads to :

1. ↓ Insulin induced suppression of hepatic glucose production
2. ↑ Fatty acid and cholesterol synthesis.
3. ↑ Hepatic VLDL production
4. ↑ Adipocyte lipolysis. (Nesto, 2004) [47].

PATHOPHYSIOLOGY OF METABOLIC SYNDROME :

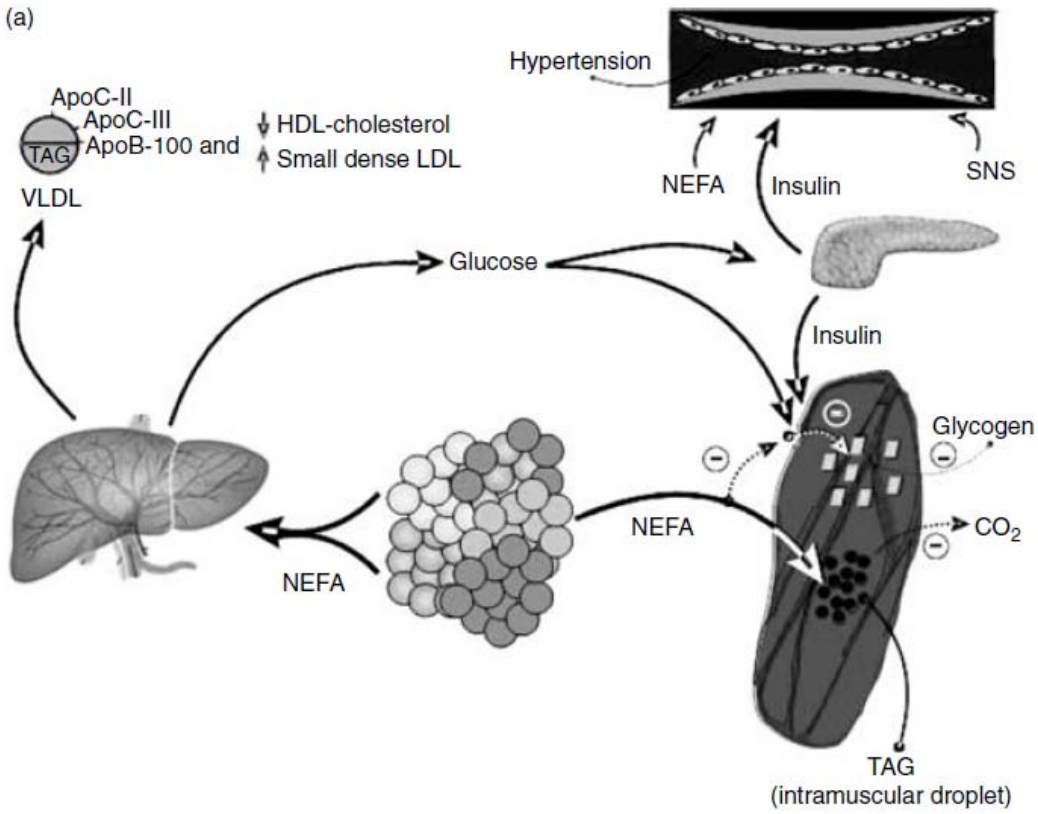


Fig 1.2

NEFA are released in abundance from an expanded adipose tissue mass. In the liver it leads to ↑ glucose & TAG production and secretion of VLDL. Associated abnormalities are ↓ HDL, ↑S-LDL-C. NEFA also reduces insulin sensitivity in muscle by inhibiting insulin mediated glucose uptake, leading on to decreased production of glycogen, ↑ Insulin Secretion resulting in hyperinsulinemia.

Hyperinsulinemia leads to sodium reabsorption and increased sympathetic nervous system activity leading to hypertension. Superimposed and contributory to IR produced by excessive NEFA is the paracrine and endocrine effect of proinflammatory state.

Increased adipocyte lipolysis leads to increased NEFAs. NEFA cause :

1. ↑ Hepatic TGL synthesis
2. ↑ Hepatic VLDL secretion
3. Reduced glucose uptake and oxidation
4. ↓ HDL
5. ↑ LDL
6. ↑ Plasma glucose

EFFECTS OF ADIPONECTIN IN METABOLIC SYNDROME [44]:

Adiponectin secreted by adipocytes have its receptors in skeletal muscle and liver.

It has beneficial effects on insulin sensitivity, fat and glucose metabolism.

It decreases the inflammatory pathway via reduction of Nuclear factor - Kappa β activity (Chandran et al.,) [7]

Insulin resistance directly leads to endothelial dysfunction by increasing expression of ICAM-1 and thereby increasing macrophage attachment to endothelium.

ROLE OF GLUCOCORTICOIDS IN METABOLIC SYNDROME :

1. Many of the properties of glucocorticoid hormones are antagonistic to the actions of Insulin.

2. Elevated plasma cortisol concentrations in morning samples are associated with High BP, glucose intolerance, Insulin resistance and hyperlipidemia. (Filipovsky et al;) [14]

3. Recent evidence suggest that foetal overexposure to increased concentrations of Glucocorticoids may influence subsequent development of metabolic syndrome in adulthood. (Langley - Evans 1997) [34].

RECENT CONCEPTS OF GENES PREDISPOSING TO METABOLIC SYNDROME :

Mutations in the PPAR γ gene that disrupt the function of protein causes severe IR, dyslipidemia and Hypertension. (Barroso et al., 1999, savage et al., 2003) [4,57]

Calpain 10 gene is important in modification and processing of proteins in the cell. Variants in calpain gene alter the risk to Type 2 DM. (Weed on et al., song et al) [59, 67].

Variants in SUR & kir 6.2 cause rare diabetes related disorders & predispose to Type 2 DM.

Mutations in HNF1 ά. HNF-4 ά and rarely in GCK gene cause MODY.

Genetic studies reveal important etiological pathways and together provide some prediction of who will or will not get disease.

There are several advantages to knowing which genes predispose to a common disease.

1. Improved knowledge of aetiology.
2. Predictive value.
3. Genetic association studies are more likely to reveal causal pathways than traditional association studies.

COMPONENTS AND CONSEQUENCES OF METABOLIC SYNDROME :

1. Visceral obesity
2. Hypertension
3. Insulin Resistance and Type 2 DM
4. Dyslipidemia
5. Atherosclerosis
6. Prothrombotic state
7. Endothelial dysfunction
8. Microalbuminuria
9. Polycystic Ovary syndrome
10. Non - alcoholic steato hepatitis.
11. Inflammatory markers
12. Obstructive sleep apnea.

1. DRIVING FORCE OF METABOLIC SYNDROME -OBESITY

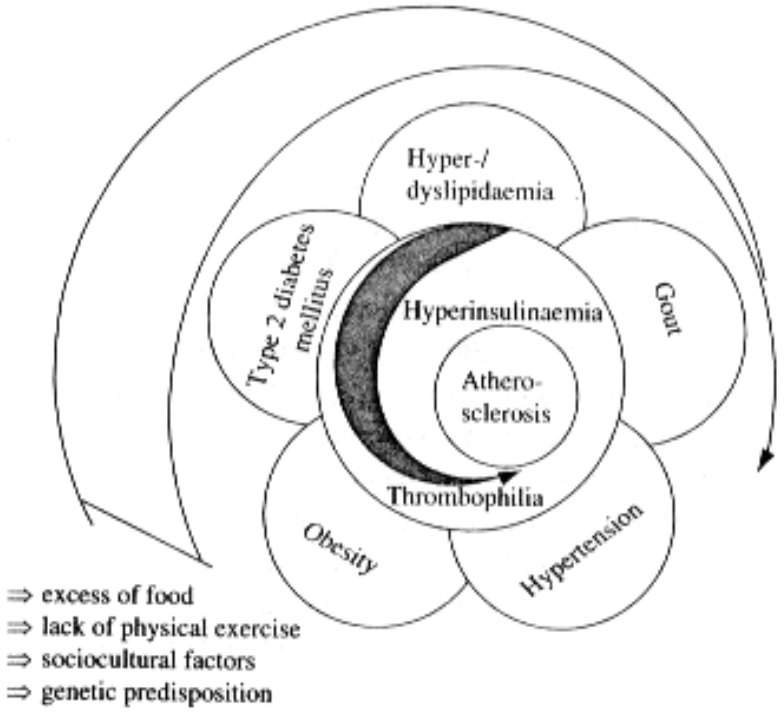


Figure 1.3 Components of the metabolic syndrome (adapted by Hanefeld M, Leonhardt W. *The Metabolic Syndrome*. Gustav Fischer, 1997)

Excess adipose tissue loaded with lipids (obesity) produces abnormal amounts of NEFA & other adipokines like adiponectin, leptin, PAI-1, resistin, TNF-α , IL - 6 and other inflammmatory cytokines. The protective adiponectin is produced in subnormal amounts in obese persons. These abnormal products of adipose tissue flood various key tissues and in turn give rise to metabolic syndrome (Source: Fustre V.O "Romke RA, Hurst's The Heart) [15]

2. HYPERTENSION :

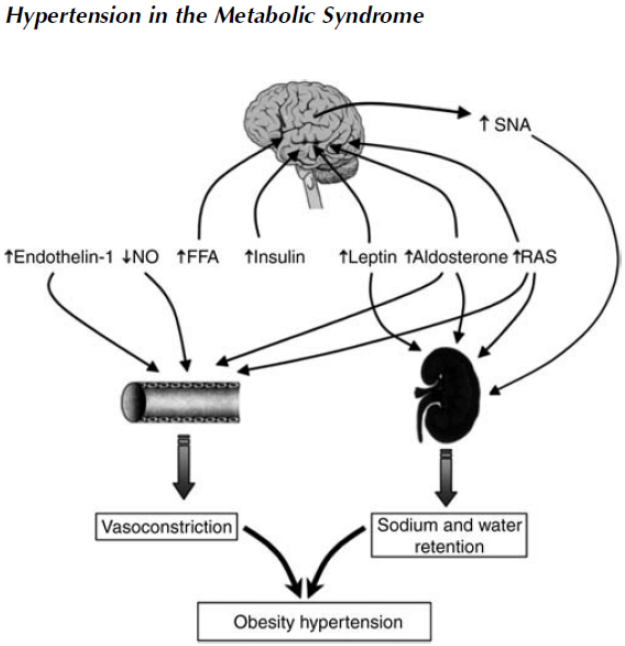


Fig 1.4

Summary of mechanisms and hormonal systems involved in obesity associated hypertension.

Cause of Hypertension in metabolic syndrome is complex and multifactorial and all of the elements of metabolic syndrome including obesity, Insulin Resistance, dyslipidemia probably are involved in mediating changes ultimately resulting in Hypertension & modifying its course

In Insulin Resistance, vasodilatory effect is lost but renal effect on sodium reabsorption is preserved.

Insulin action on increasing sympathetic nervous system activity is also preserved.

There is also a pathway specific inhibition of phosphatidylinositol - 3 - kinase signaling leading to imbalance in production of Nitric Oxide and Secretion of endothelin-1 contributing to decreased blood flow.

3. INSULIN RESISTANCE & TYPE 2 DM [19,20]:

Large number of epidemiological studies have shown that there is a relationship between low birth weight and subsequent risk of developing Type 2 DM, Insulin resistance and other features of metabolic syndrome such as Hypertension.

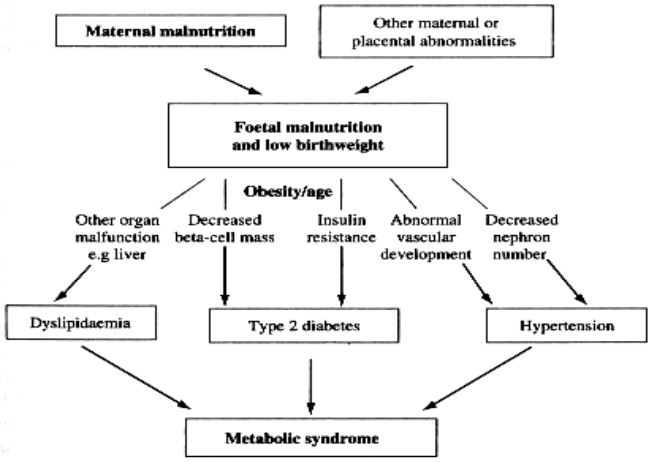


Figure 1.5 Schematic representation of the thrifty phenotype hypothesis, showing the vital role of foetal nutrition in the development of the metabolic syndrome (adapted from Hales and Barker 1992)

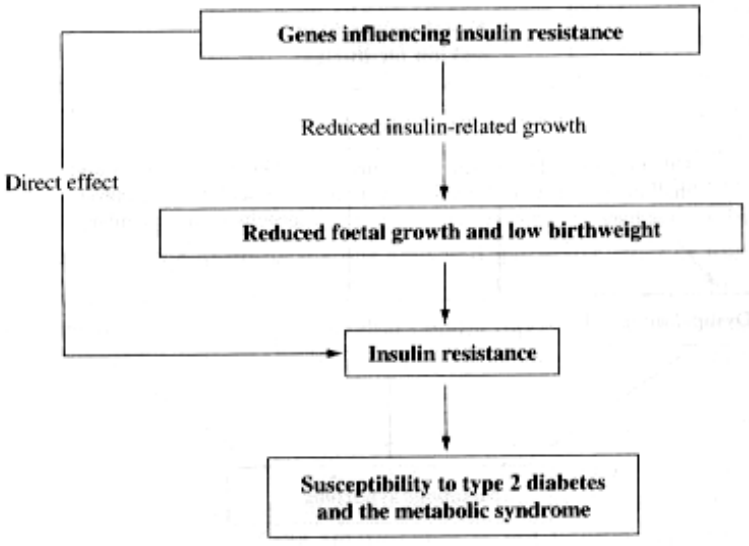
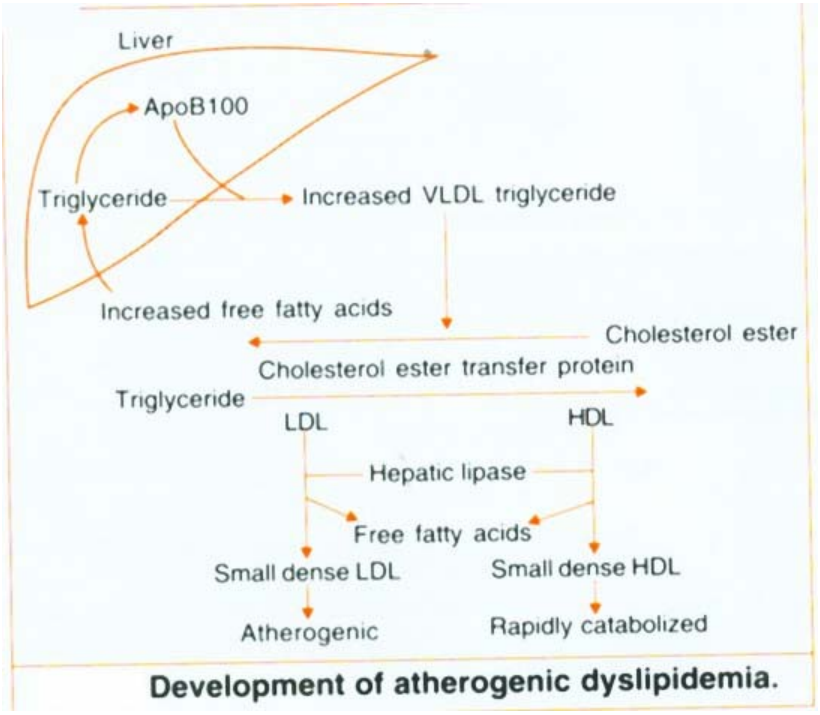


Figure 1.6 The foetal insulin hypothesis (adapted from Hattersley and Tooke)

4. DYSLIPIDEMIA :



Development of atherogenic dyslipidemia.

↑ NEFA → Portal Venous System → Liver → ↑ VLDL ↑ TAG

↑ VLDL is also due to decreased degradation or inhibition of microsomal Trigylceride Transfer Protein Activity - a protein needed for VLDL assembly process[46].

HDL particles become Triglyceride rich and hydrolysed by Hepatic lipase leading to small dense HDL 3 or large HDL2. HDL3 is atherogenic, HDL2- is antiatherogenic.

↑ VLDL leads to ↑ small dense LDL.

Reduced affinity of small dense LDL to LDL receptors leads to prolongation of circulation time for this particle. It is highly atherogenic.

Insulin resistance is also associated with ↓ clearance of lipids.

↑ in Hepatic lipase leads to ↑ clearance of HDL

5. ATHEROSCLEROSIS :

Inflammation is the bridging link between atherosclerosis & metabolic syndrome [9].

Chronic inflammation → endothelial dysfunction. This facilitates interaction between modified lipoproteins, monocyte derived macrophages, T cells and normal cellular elements of vessel wall, leading on to early and late atherosclerotic process[45].

Metabolic syndrome is a chronic low grade inflammatory condition in which inflammation impairs insulin action through various mechanisms. Other components of Metabolic syndrome also accelerates atherosclerosis.

6. PROTHROMBOTIC STATE :

Metabolic syndrome is associated with a significant increase in the risk of developing prothrombotic state, due to disruption in the balance of factors regulating coagulation and fibrinolysis [28].

There is an increase in levels of many clotting factors Fibrinogen, Factor VII, VIII, XII & XIIIB subunit[13].

Fibrinolytic system is relatively inhibited due to the increase in levels of plasminogen - Activator Inhibitor I.

Platelets in metabolic syndrome patients are resistant to actions of Insulin, Nitric Oxide and PG I2 thereby upregulating aggregation.

All these, favour development of hypercoagulable prothrombotic state enhancing cardiovascular disease risk. (Jugan vague., et al) [28]

7. ENDOTHELIAL DYSFUNCTION :

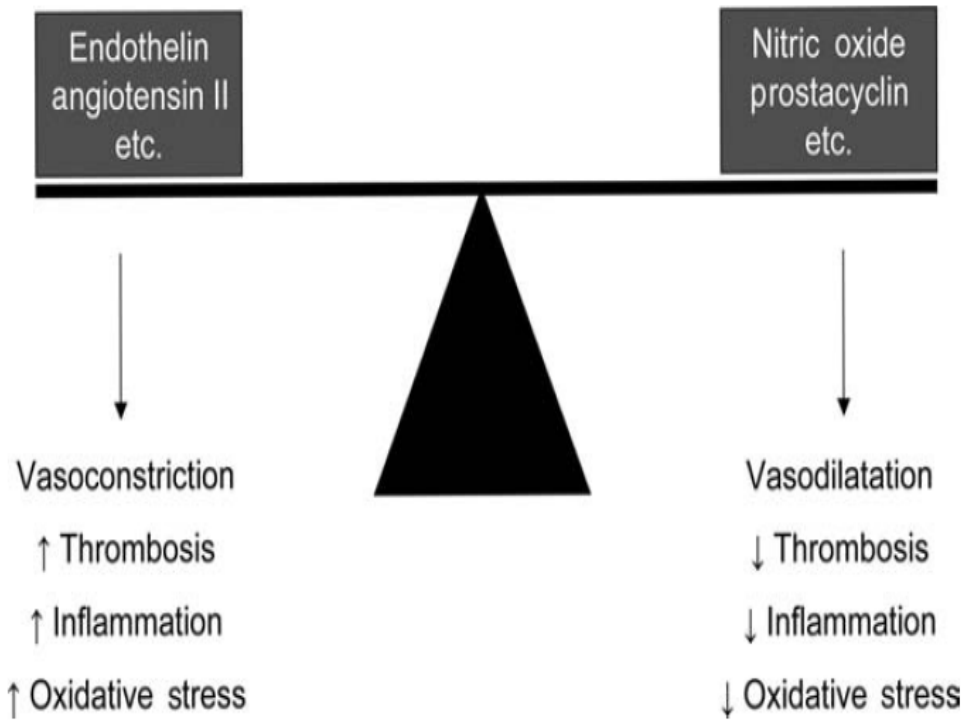


Fig 1.7

In metabolic syndrome, there is abnormal Nitric Oxide metabolism that leads on to decreased endothelial Nitric Oxide production. (Venugopal et al) [64]

There is a reduced vasodilatory response to Insulin. Tack et al., 1998) [62]

Increased oxidative stress, inflammation and thrombosis are the consequences of vasoconstriction due to increased endothelin and Angiotensin. Abnormal nitric oxide metabolism also favours vasoconstriction.

8. MICROALBUMINURIA :

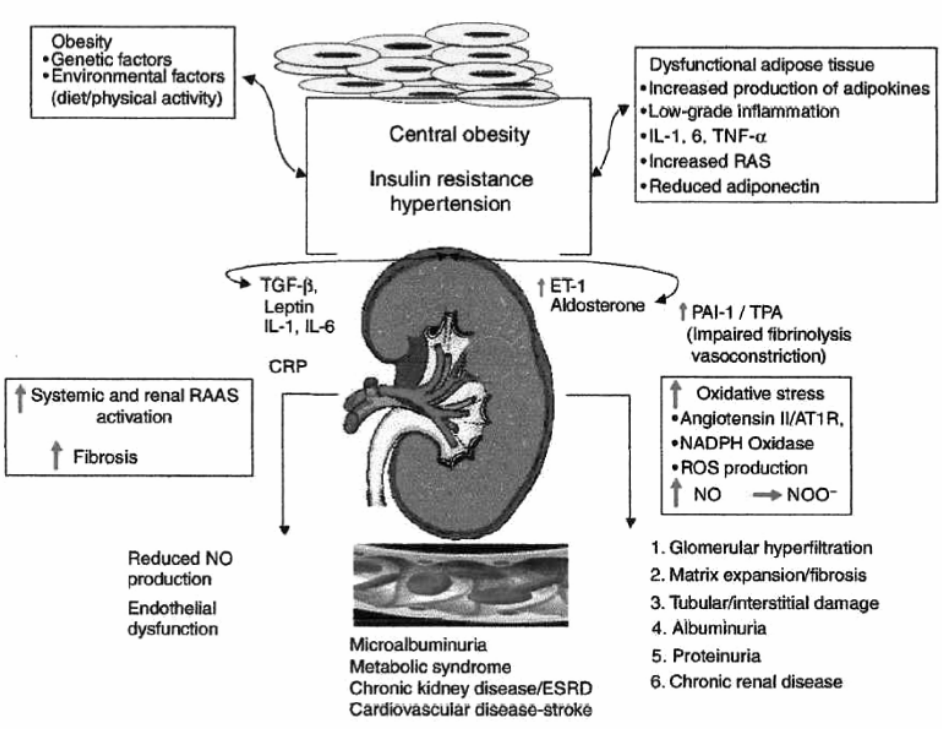


Fig 1.8

Mechanisms leading to microalbuminuria in metabolic syndrome [36].

9. POLYCYSTIC OVARY SYNDROME[23,30]:

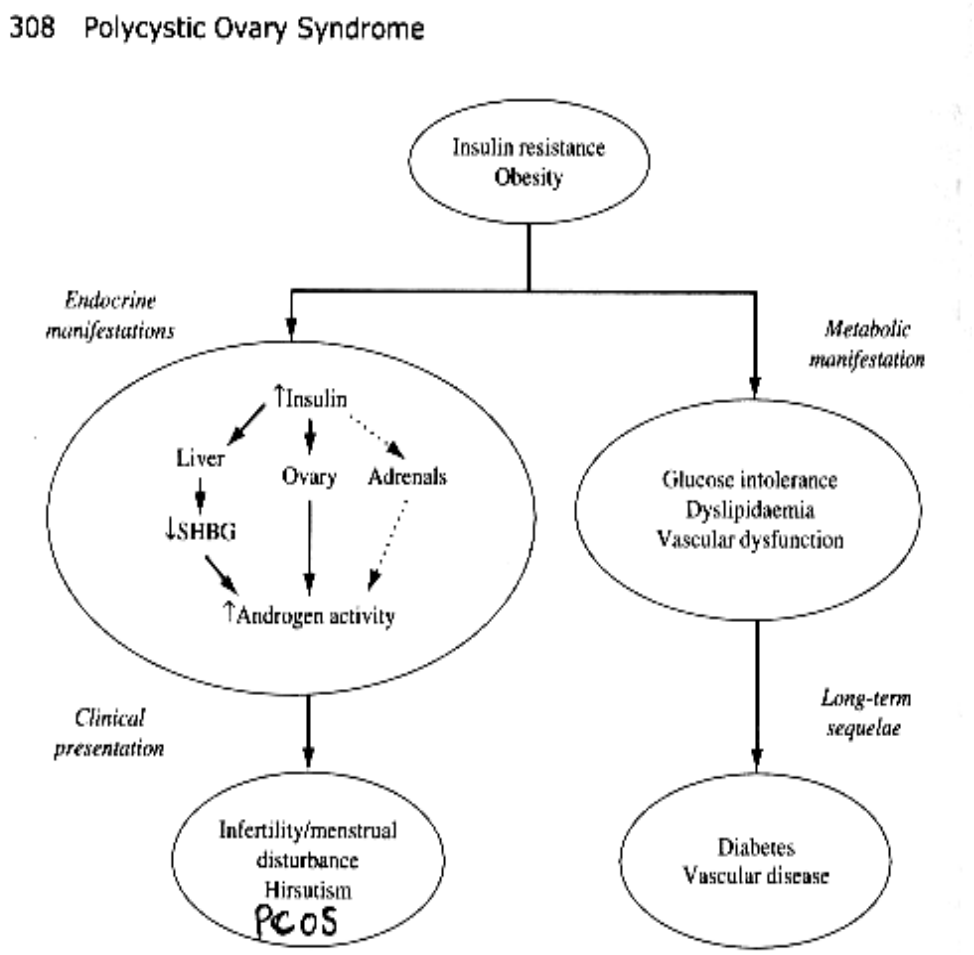


Figure 1.9 The postulated consequences linked to insulin resistance in women with polycystic ovary syndrome

The etiological mechanisms underpinning IR and reproductive abnormalities in women with PCOS are

1. Genetic contributions to both reproductive and metabolic features.
2. Defects in adipose tissue lipolytic cascades.
3. Inflammation mediators leading to IR.
4. Foetal programming effects.

10. NON - ALCOHOLIC STEATO HEPATITIS [37, 69]:

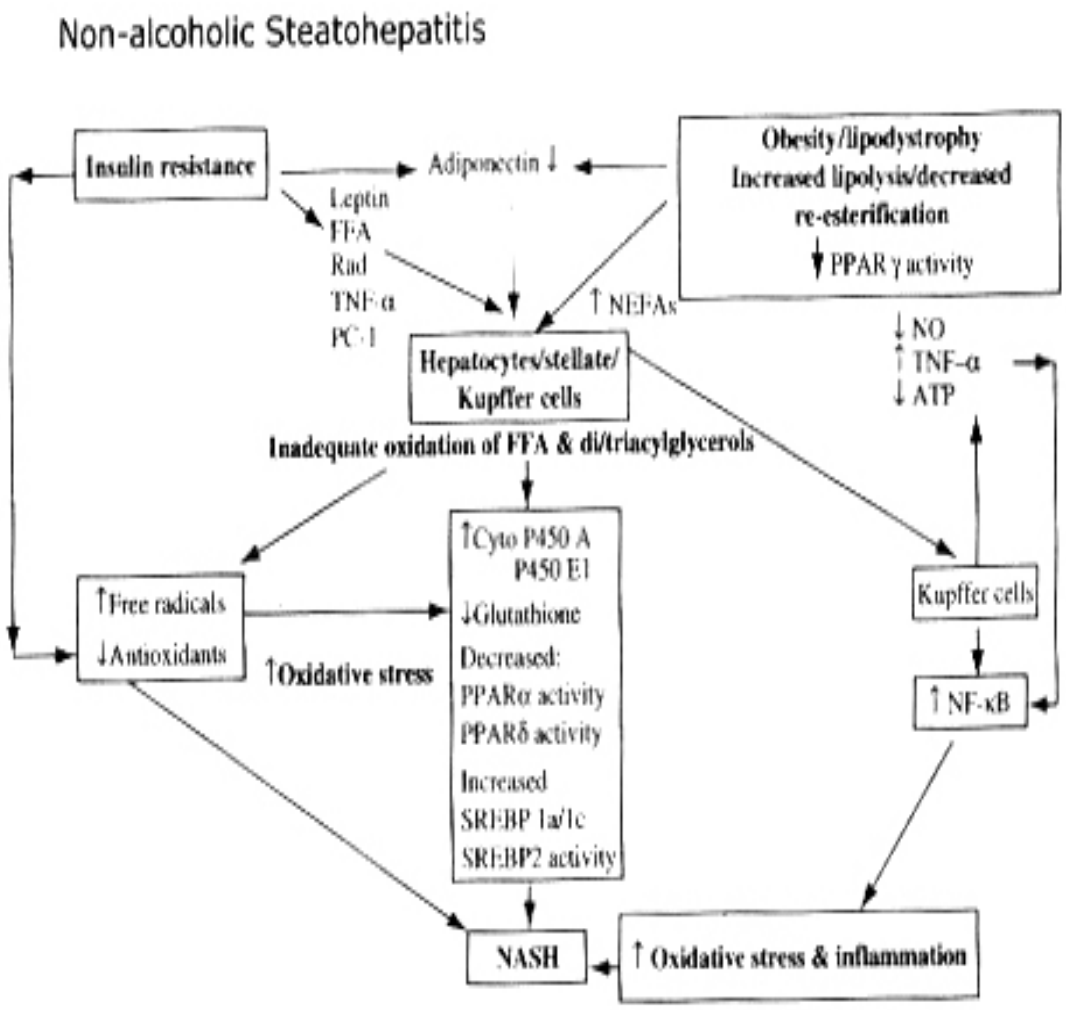


Figure 1.10 Scheme showing possible pathways involved in the pathogenesis of non-alcoholic steatohepatitis (NASH) in the metabolic syndrome

Non-alcoholic steatohepatitis (NASH) can be defined as significant steatohepatitis that is not the result of alcohol, drugs or any other single identifiable cause. Importantly, there is invariably an association with Insulin resistance.

11. INFLAMMATORY MARKERS :

There is an increase in proinflammatory cytokines including IL-1, IL-6, IL-18, Resistin, TNFά, CRP due to overproduction by the adipose tissue derived macrophages.

Among these markers, CRP predicts the development of MetS and cardiovascular disease risk more than others.

12. OBSTRUCTIVE SLEEP APNEA :

Obstructive sleep apnea is commonly associated with obesity, Hypertension, Increased cytokines, Impaired glucose tolerance and Insulin resistance.

It is frequently seen in metabolic syndrome patients. continuous positive airway pressure treatment improves Insulin sensitivity.

Current Challenges in metabolic syndrome :

- The syndrome is not a discrete entity known to be caused by a single factor. It shows considerable variation in the components among different individuals. This variation is even greater among different racial and ethnic groups.
- At present no unifying mechanism can explain MetS. Consequently, there is no unique treatment for it. Treatment strategies will need to address unique risk factors in individual patients, rather than setting goals in an aggregate syndrome.

COMMON SOIL PATHOGENESIS FOR METABOLIC SYNDROME :

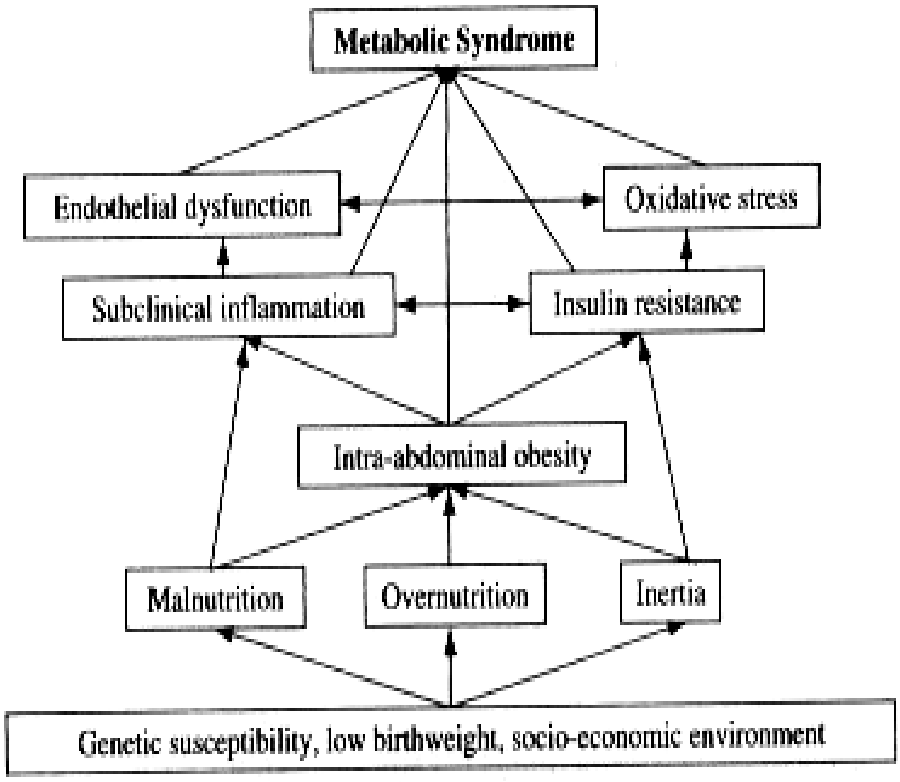


Figure 1.11 'Common soil' in the pathogenesis of the metabolic syndrome

Insulin resistance, intra-abdominal obesity and low grade inflammation are accepted parts of the 'Common Soil' of the metabolic syndrome.

CURRENT CLINICAL DIAGNOSIS OF METABOLIC SYNDROME [8,58]

NCEP ATP IIII (≥3 Criteria)	AHA/NHLBI (3 Criteria)	IDF (Obesity + ≥other criteria)	WHO (Insulin Resistance +≥ 2Other criteria)
WAIST CRICUMFERENCE			**Body Mass Index**
>40 inch(102 cm) (men) > 35 inch(88 cm) (women)	≥ 40 inch (men) ≥ 35 inch (female)	Ethnicity Specific Ethnicity Specific	> 30 kg / m2 and / or WHR > 0.9 (men) >0.85 (women)
TRIGLYCERIDES			
> 150 mg/dl	> 150 mg/dl or treatment for hypertriglyeridemia	≥ 150mg / dl or treatment for hypertriglyceridemia	≥ 150 mg / dl
HIGH DENSITY LIPOPROTEIN CHOLESTEROL (HDL - C)			
< 40 mg / dl (men) <50 mg / dl (women)	< 40 mg / dl (men) < 50mg / dl (women) or On treatment for Low HDL-C.	< 40 mg / dl (men) < 50 mg / dl (women) or on treatment for low HDL-C	< 35 mg / dl (men) <40 mg/dl (women)
BLOOD PRESSURE			
≥ 130/ 85 mm Hg or on treatment for HTN	≥ 135/85 mmHg (or) on treatment for HTN	≥ 130 / 85 mm Hg or on treatment for HTN.	≥ 140/90 mm Hg (or) on treatment for HTN
FASTING GLUCOSE			**INSULIN RESISTANCE**
100-125 mg/dl	≥ 100mg / dl (or) on treatment for Hyperglycemia	≥ 100mg / dl (or) diagnosis of DM	Type 2DM, IFG, IGT
			URINARY ALBUMIN
			> 20 mg/ ml
			ALBUMIN CR RATIO
			> 30 mg / g

Ethnicity specific Waist circumferences

European	:	Men ≥ 94 cm, Women ≥ 80 cm;
South Asians	:	Men ≥ 90cm, Women ≥ 80 cm;
Chinese	:	Men ≥ 90 cm,Women≥ 80cm;
Japanese	:	Men ≥ 85 cm, Women ≥ 90 cm,
South & central American	:	Men ≥ 90 cm, Women ≥ 80 cm,
Subsaharan Africans	:	Men ≥ 94 cm, Women ≥ 80 cm,
Eastern Meditteranean & Middle east	:	Men ≥ 94, Women ≥ 80cm,
Adapted from	:	Cleveland Clinic Journal of Medicine, Volume 74, Number3, Page 199-208, March - 2007.

MANAGEMENT OF METABOLIC SYNDROME :

Management of Lifestyle risk factors[8,21,58] :

1. Abdominal obesity [8] :

Weight reduction -

1) Reduced caloric intake & increased physical activity.
2) Behaviour Changes
3) Currently available weight loss drugs are of limited utility
4) Bariatic surgery in severely obese.

2. Physical Inactivity [58] :

1. Practice 30 minutes of moderate intensity exercise, preferably on all days of the week.
2. Even more exercise adds more benefit

3. Atherogenic & Diabetogenic diets [21] :

Diet should be low in saturated fats, trans fats, cholesterol, sodium and simple sugars.

There should be ample intake of fruits, vegetables, whole grains and fish. Total fat content in daily diet should be 25 to 35 %

MANAGEMENT OF METABOLIC RISK FACTORS[8,21,58]:

1. Atherogenic dyslipidemia:

1. Statins lower both LDL - C & non - HDL – C.
2. Both fibrates & Nicotinic Acid reduce Non - HDL - C. Combination of these three drugs is an option.
3. Among fibrates, fenofibrate is preferable as it produces less myopathy when compared to gemfibrozil.

2. Elevated BP :

1. Life style therapies : Weight reduction, increased physical activity, alcohol moderation, sodium reduction, increased consumption of fresh fruits, vegetables, low fat dairy products.
2. First line antihypertensives - ACE inhibitor.
3. In those who cannot tolerate ACEI, ARBS can be given.

3. Elevated fasting glucose :

1. Life style therapies
2. Metformin, thiazolidinediones, acarbose lower the risk for Type 2 DM in people with IFG or IGT.

4. Prothrombotie State :

Only available long term approach to counter prothrombotic state is low dose aspirin or other antiplalelet agents.

5. Pro inflammatory State :

1. Measurement of CRP is the simplest way to identify a proinflammatory state in clinical practice.

2. Life style changes especially weight reduction reduces CRP levels.

3. Statins, Nicotinic acid, fibrates, ACE inhibitors, thiazolidinediones are reported to reduce CRP levels. At present, these drugs cannot be recommended specifically to reduce a proinflammatory state independent of their indications for other risk factors.

CAD AND METABOLIC SYNDROME :

Coronary artery disease is typically defined as a >50 % stenosis of any epicardial coronary artery most commonly due to obstruction by atheromatous plaques [2,3].

Manifestations of CAD include stable angina, acute coronary syndrome, congestive heart failure, sudden cardiac death and silent ischemia.

Metabolic syndrome with its clustered riskfactors is known to promote or increase the risk of development of cardiovascular disease.

Applying Framingham global risk algorithms to U.S.Populations with metabolic syndrome but without Diabetes, 45 % of men and 42% women were found to be at intermediate risk (10-20%) of CAD another 20 % of men & 2% of women at high risk (>20%) of CAD in the next 10 years.

CVA AND METABOLIC SYNDROME :

Stroke is the abrupt onset of neurologic deficit that correspond to interruption of vascular supply to a specific brain region. A stroke may be ischemic or haemorrhagic.

The most recent definition of stroke for clinical trials has required either symptoms lasting > 24 hours or imaging of an acute clinically relevant brain lesion in patients with rapidly vanishing symptoms[1].

After adjustments for age, sex, history of CAD & CRP level, individuals with metabolic syndrome were more than twice as likely as those without it to show evidence of silent brain infarctions on MRI.

Metabolic syndrome is associated with intracranial and extracranial atherosclerotic disease. Individuals with MetS have an increased prevalence of carotid intima - media thickness, asymptomatic carotid atherosclerotic plaques, and leukoaraiosis in healthy.

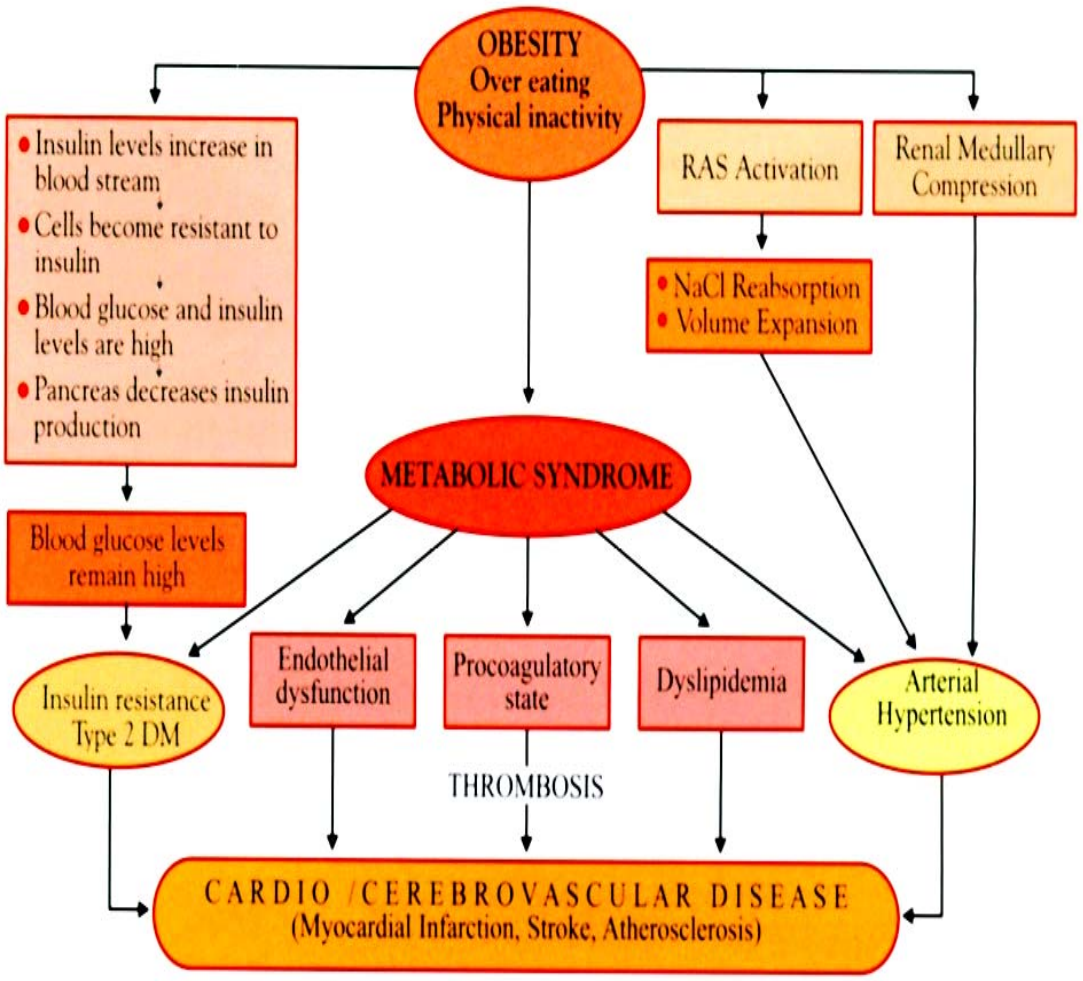


Figure 1: Metabolic Syndrome: Constellation of Metabolic Abnormalities Linked to Insulin Resistance

DM Diabetes mellitus; RAS = Renin angiotensin system

Fig 1.12

Thus, all the consequences of metabolic syndrome like Insulin Resistance, Type 2 DM, endothelial dysfunction, procoagulatory state, dyslipidemia and Arterial hypertension leads on to thrombosis and finally contribute to the development of coronary Artery disease and cerebrovascular accidents.

MATERIALS AND METHODS :

This study was conducted in Thanjavur Medical College Hospital, Thanjavur, Tamil Nadu. The study was conducted in the Department of Internal Medicine. The Study period extended between June 2007 to October 2008.

All patients were thoroughly evaluated with a detailed history and appropriate investigations as per proforma. Metabolic syndrome in study subjects was diagnosed as per NCEP : ATP III 2001 criteria.

INCLUSION CRITERIA :

1. 50 Patients who had ECG and ECHO findings suggestive of coronary Artery disease.

2. 50 Patients who had clinical & CT scan findings of cerebrovascular accident.

3. Already known dyslipidemic, hypertensive & diabetic were also included.

4. Patients who smoke and consume alcohol.

5. Patients with family history of dyslipidemia, diabetes, Hypertension, CAD & CVA.

Exclusion Criteria:

1. Valvular Heart disease

2. Schizophrenic Patients

3. Patients on Antipsychotics, antiretroviral therapy

4. Patient on oral contraceptives.

5. Patients with meningitis.

6. Systemic Malignancy, Nephrotic syndrome

8. Patients with vasculitis.

METHODS :

To measure waist cirumference, top of right iliac crest located. A measuring tape was placed in a horizontal plane around abdomen at level of iliac crest. Before reading measurement, it is estimated that the tape is snug but does not compress the skin and is parallel to floor. Measurement was at the end of normal expiration.

Blood samples for fasting blood glucose were taken after eight hours overnight fast.

Blood samples for lipid profile were taken after 12 hours overnight fast.

Blood pressure was recorded in right upper limb with patient in sitting posture and for CVA patients it was recorded in supine posture.

LIMITATIONS OF THE STUDY :

Age specific prevalence rates may not reflect exact prevalence in general CAD & CVA patients.

Prevalence of Hyperinsulinemia was not determined in this study as serum Insulin measurement is not a criteria for diagnosis of Mets as per NCEP : ATP III .

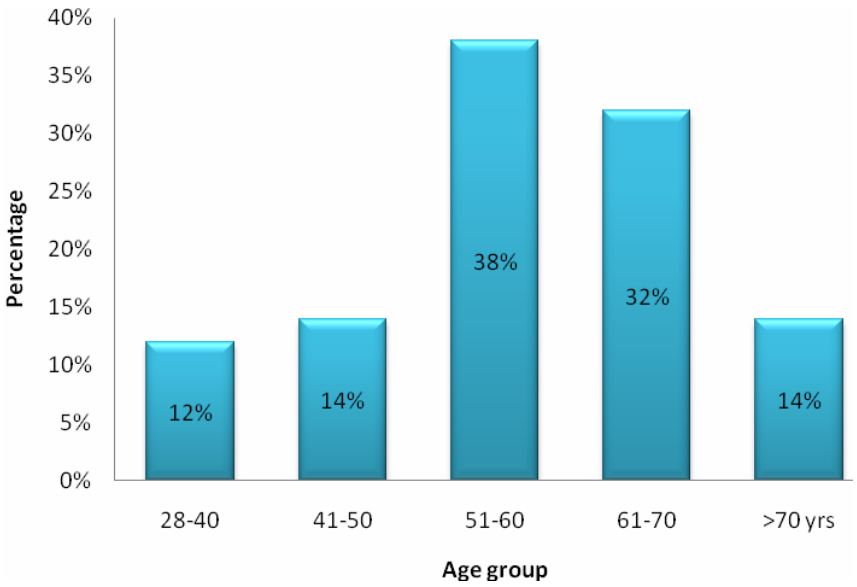
Waist circumference in most of the stroke patients could only be measured in supine posture.

RESULTS

I. AGE DISTRIBUTION IN CAD PATIENTS:

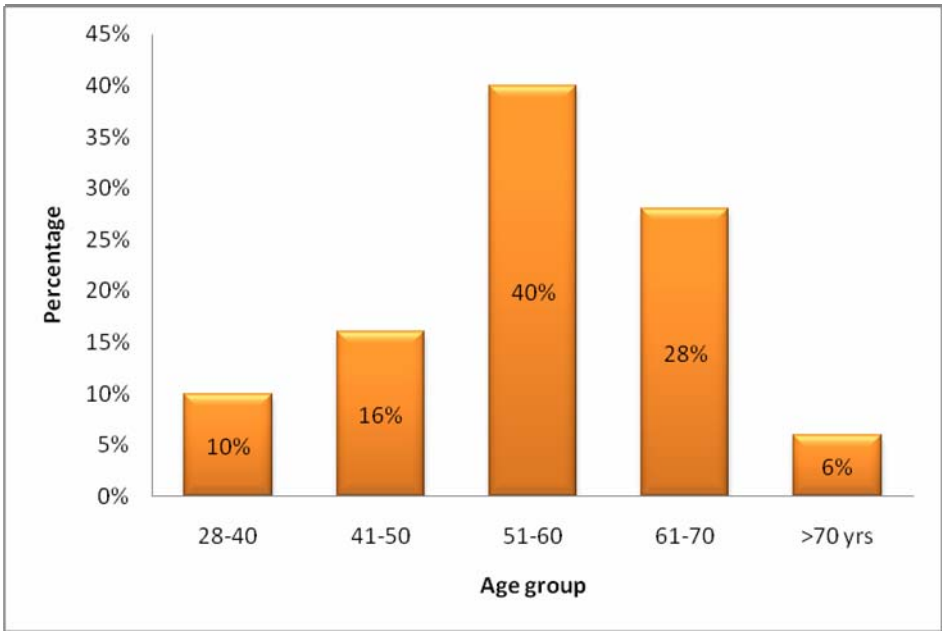
Totally 50 CAD patients were included in this study.Age distribution among them is as follows:

S.No	Age group	No of Patients	Percentage
1.	28-40	6	**12 %**
2.	41-50	7	**14 %**
3.	51-60	19	**38 %**
4.	61-70	11	**32 %**
5.	**>70 yrs**	**7**	**14%**



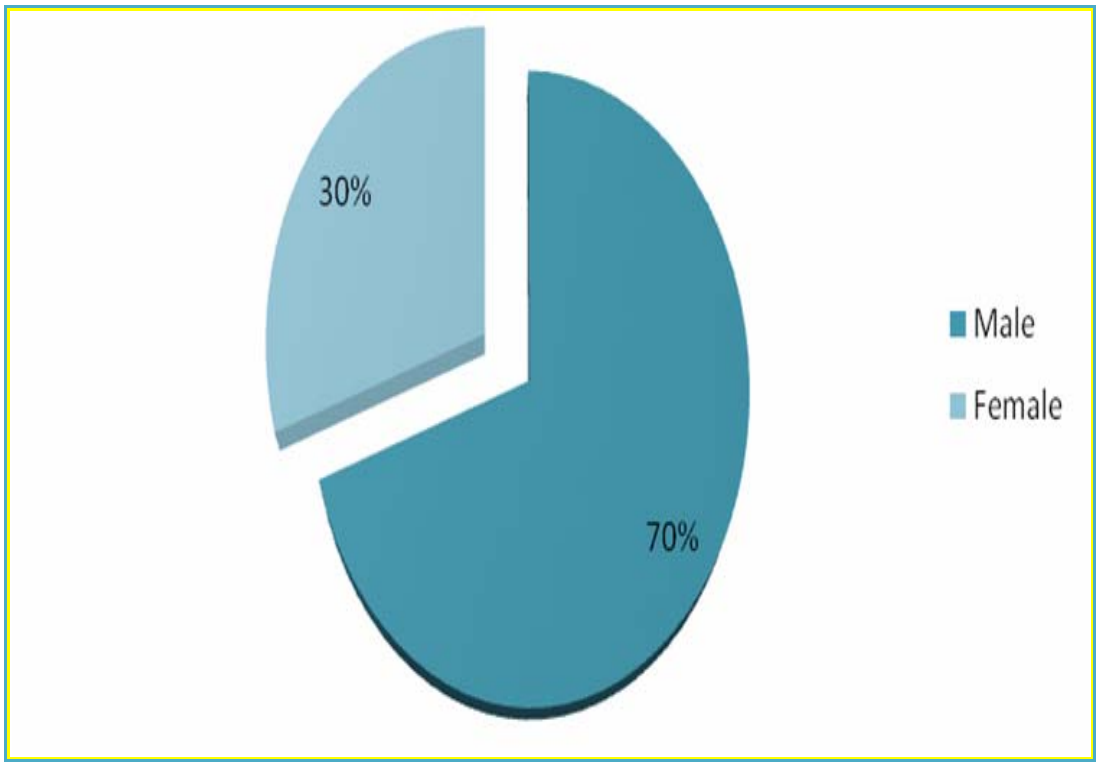
II. AGE DISTRIBUTION IN CVA PATIENTS:

S.No	Age group	No of Patients	Percentage
1.	28-40	5	**10 %**
2.	41-50	8	**16 %**
3.	51-60	20	**40 %**
4.	61-70	14	**28 %**
5.	**>70 yrs**	**3**	**6%**



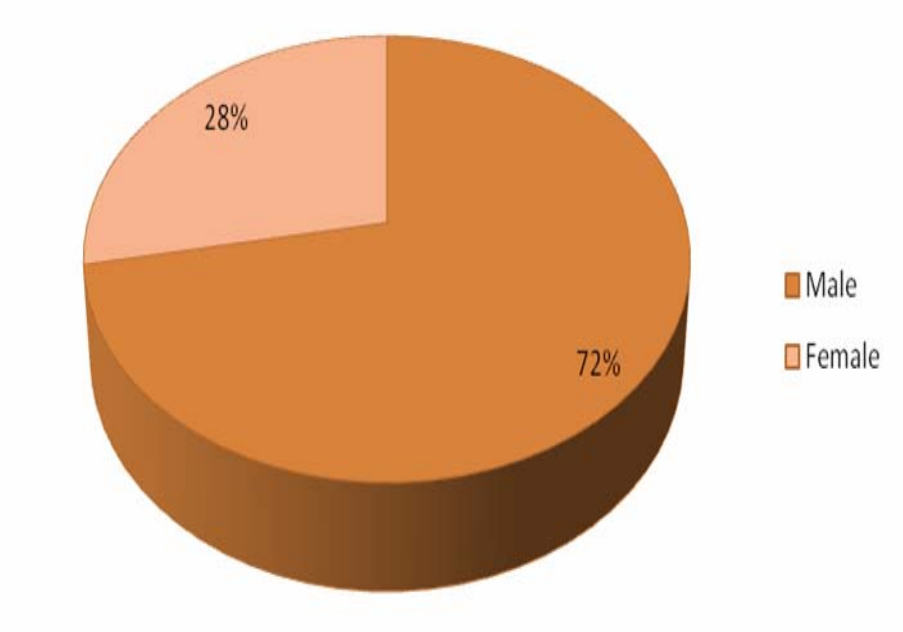
III. SEX DISTRIBUTION IN CAD PATIENTS :

Sex	Number of Patients	Percentage
Male	35	**70 %**
Female	**15**	**30 %**



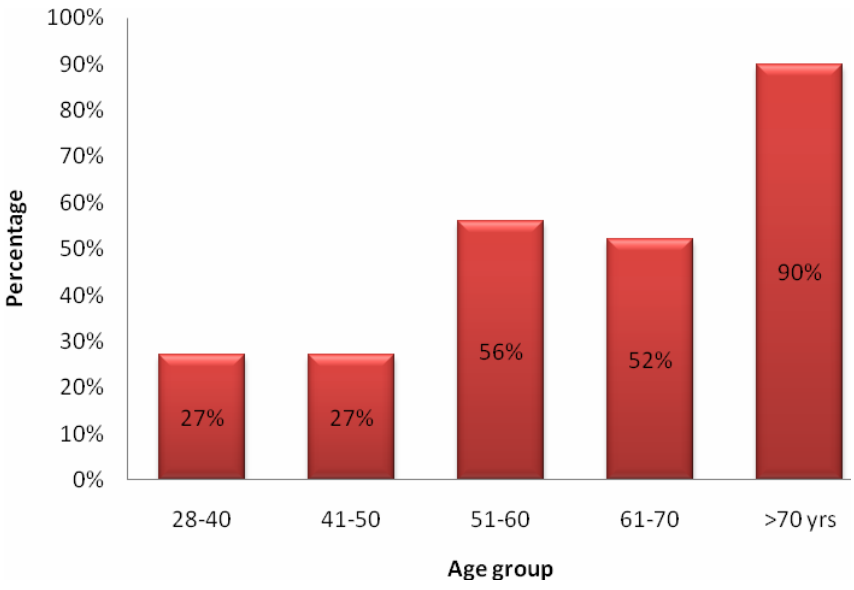
IV. SEX DISTRIBUTION IN CVA PATIENTS :

Sex	Number of Patients	Percentage
Male	36	**72 %**
Female	**14**	**28 %**



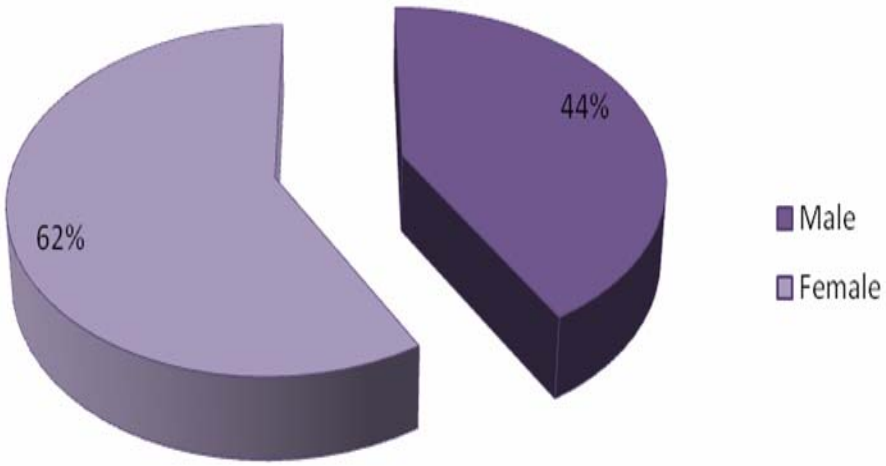
V. AGE SPECIFIC PREVALENCE OF METABOLIC SYNDROME IN CAD AND CVA PATIENTS:

S.No	Age	Number of Patients	Metabolic syndrome patients	Percentage
1.	28-40	11	3	**27%**
2.	41-50	15	4	**27%**
3.	51-60	39	22	**56%**
4.	61-70	25	13	**52%**
5.	**>70**	**10**	**9**	**90%**



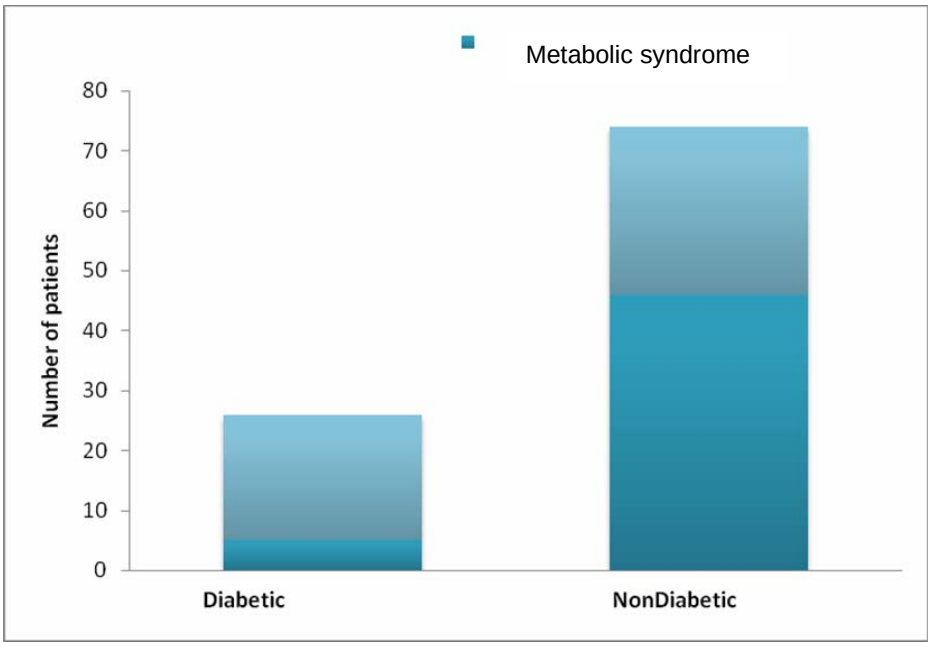
VI. SEX SPECIFIC PREVALENCE OF METABOLIC SYNDROME IN CAD & CVA PATIENTS

Sex	No of Patient	Metabolic Syndrome patients	Percentage
Male	71	31	**44%**
Female	**29**	**18**	**62%**



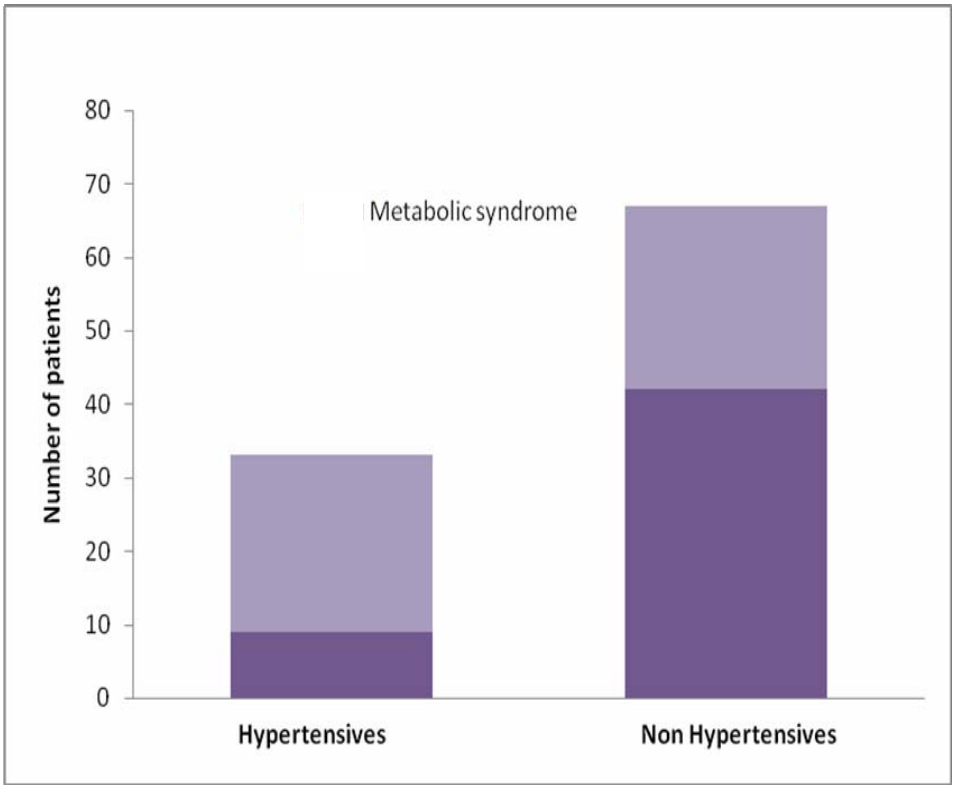
VII. PREVALENCE OF METS IN DIABETES AND NON-DIABETIC PATIENTS :

Group	No of Patients	No of Mets Patients	Percentage
Diabetic	26	21	**81%**
Nondiabeitc	**74**	**28**	**38%**



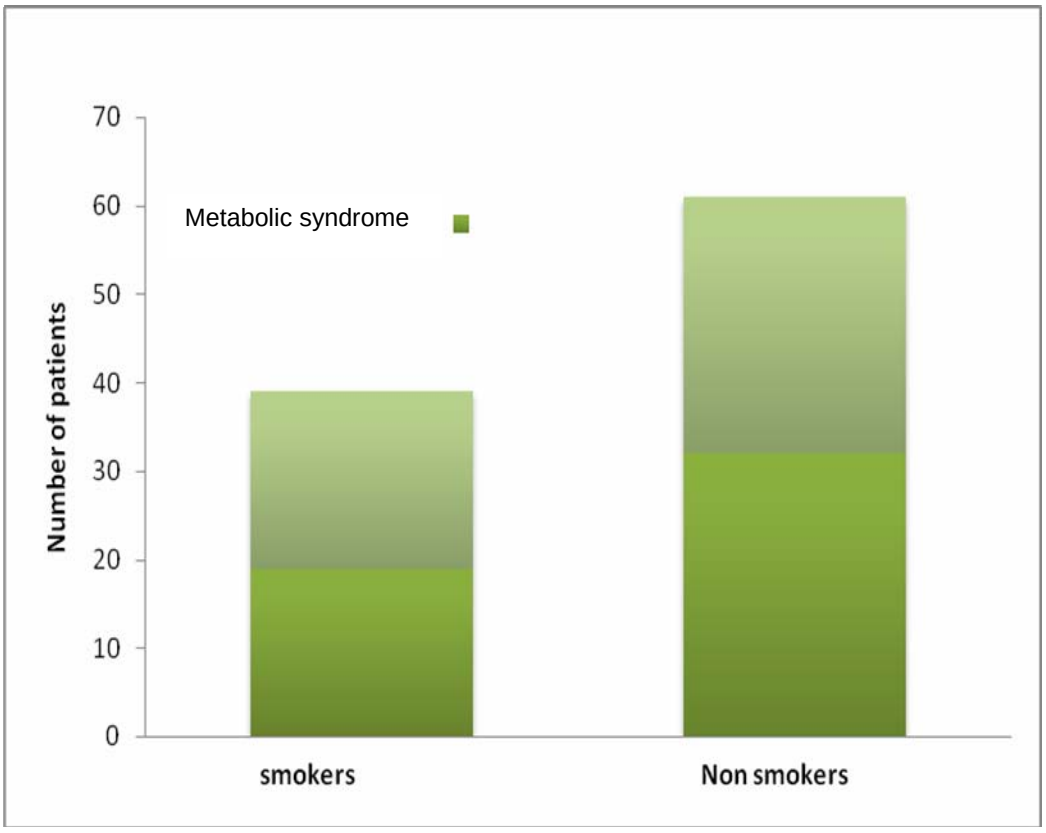
VIII. PREVALENCE OF METABOLIC SYNDROME IN HYPERTENSIVE & NON-HYPERTENSIVES.

Group	No of Patients	No of Mets Patients	Percentage
Hypertensive	33	24	**73%**
Non - Hypertensive	**67**	**25**	**37%**



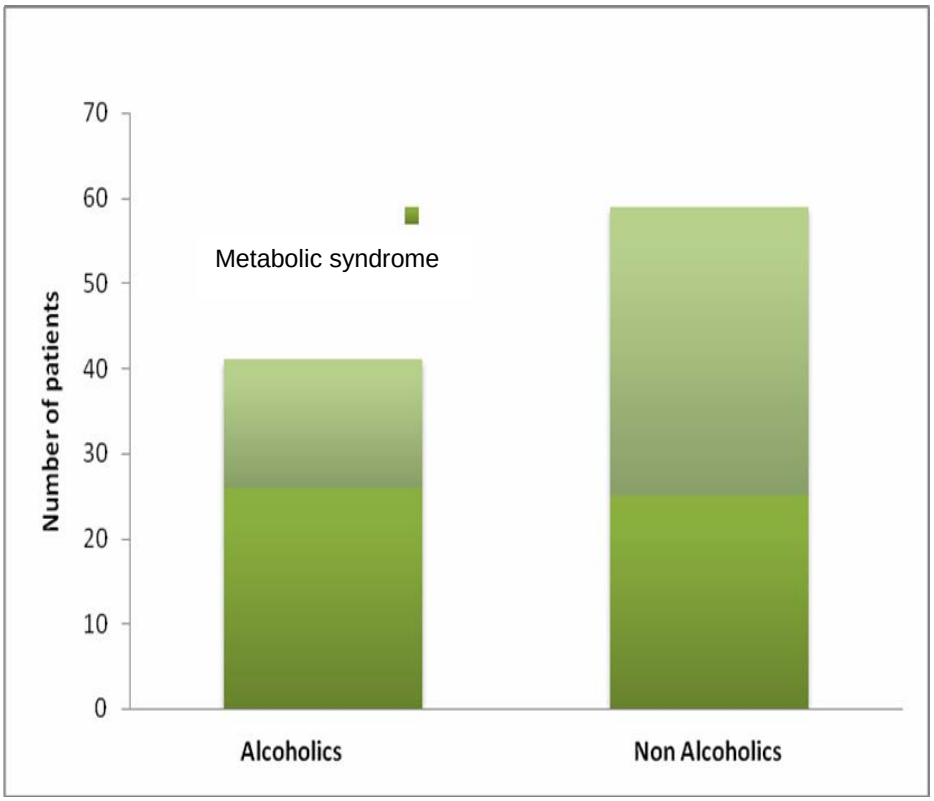
IX. METABOLIC SYNDROME IN SMOKERS :

Group	No of Patients	No of Mets Patients	Percentage
Smokers	39	20	**51%**
Non- Smokers	**61**	**29**	**47%**



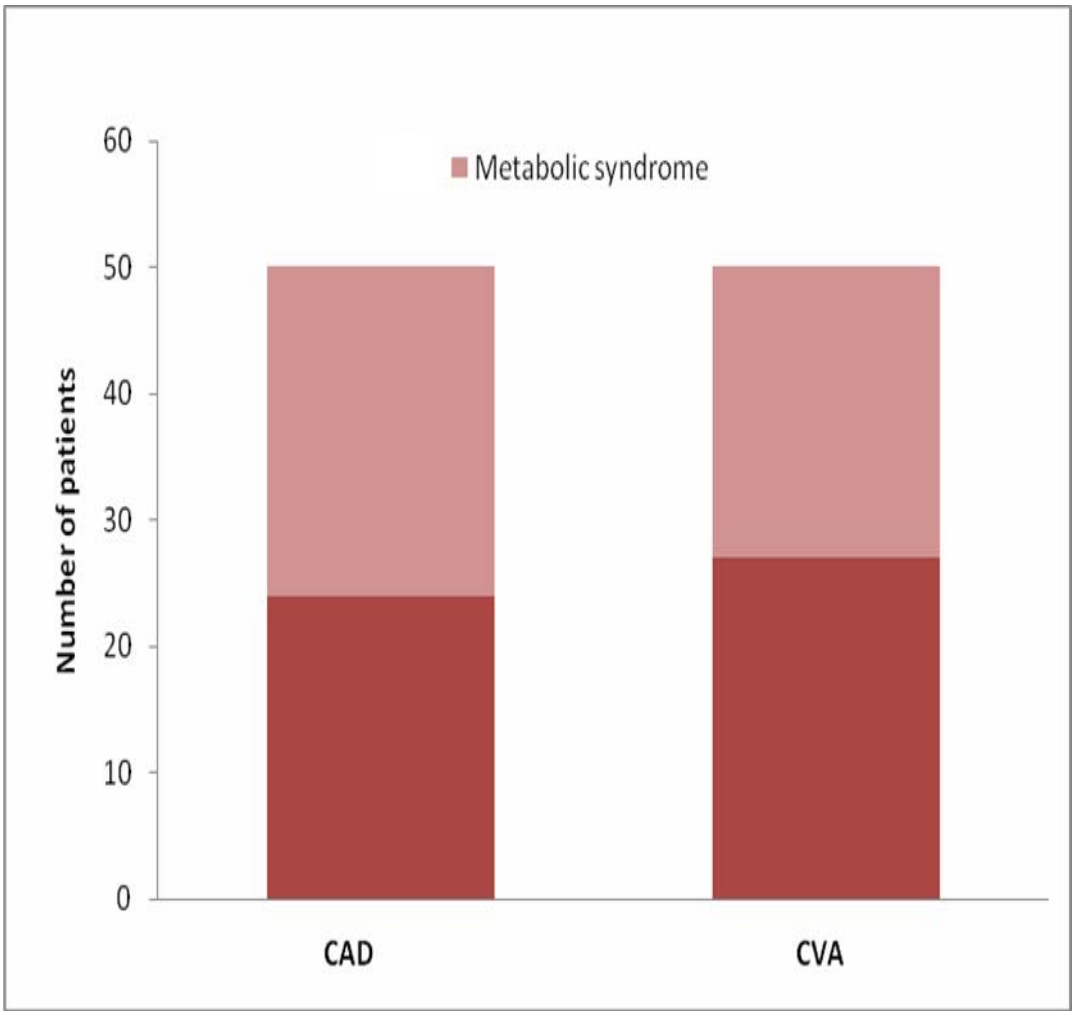
X. METABOLIC SYNDROME IN ALCOHOLICS :

Group	No of Patients	No of Ms Patients	Percentage
Alcoholics	41	15	**37%**
Non alcoholics	**59**	**34**	**58%**



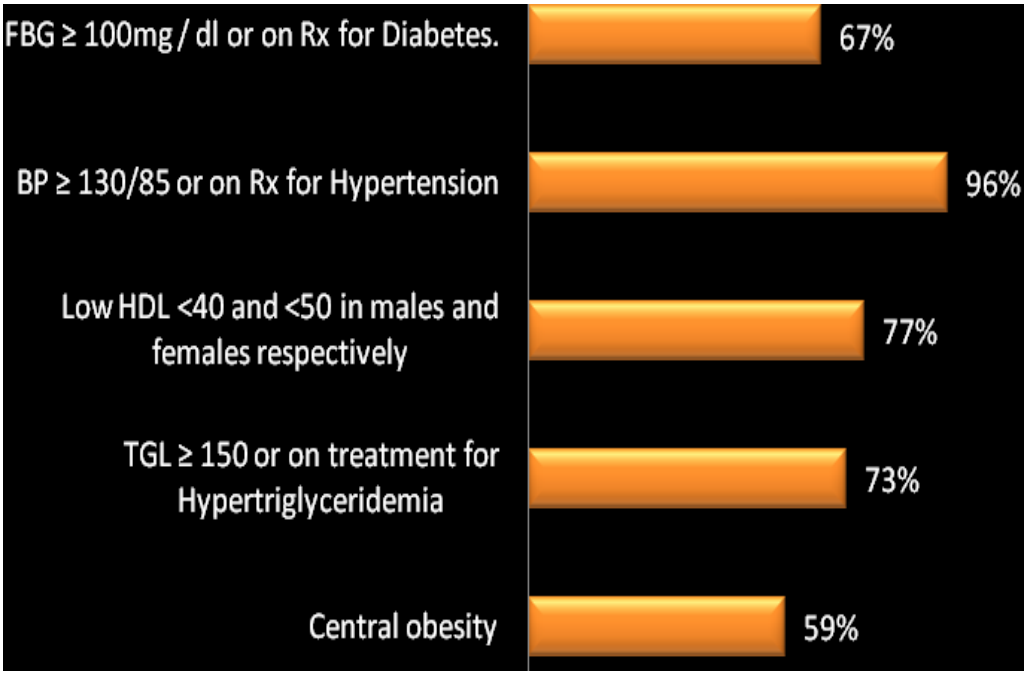
XI. PREVALENCE OF METS IN CAD & CVA PATIENTS

Group	No of Patients	No of Mets Patients	Percentage
CAD	50	26	**52%**
CVA	**50**	**23**	**46%**



XII. PREVALENCE OF INDIVIDUAL RISK FACTORS IN METABOLIC SYNDROME PATIENTS:

Risk Factor	Male	Female	Total
Central obesity	48%	78%	**59%**
TGL ≥ 150 or on treatment for Hypertriglyceridemia	61 %	94%	**73%**
Low HDL <40 and <50 in males and females respectively	77%	77%	**77%**
BP ≥ 130/85 or on Rx for Hypertension	74%	94%	**96%**
FBG ≥ 100mg / dl or on Rx for Diabetes.	**74%**	**56%**	**67%**



DISCUSSION :

TABLE 1:

AGE DISTRIBUTION IN CAD PATIENT :

In this study, it is observed that the number of coronary Artery disease patients increase as the age advances.

This observation is supported by studies of :

Sumita Dadani MD [60], MS from Department of Epidemiology. She has shown in her study that age ≥ 40 is independently associated with coronary artery disease.

Melissari M.Balbi et al., [43]

Miloo M.Edwards [44] in contemporary cardiology

TABLE : 2

AGE DISTRIBUTION IN CVA PATIENTS

In this study, it is observed that cerebrovascular accidents were more common in the patients as their age increases.

This observation is supported by

Heart and stroke statistical update by AHA[21] stroke statistics In : 2001. It says that stroke can occur at any age, but it is primarily a disease of older people. Starting at age 55, the risk of stroke doubles in each successive decade of life.

TABLE 3 AND 4

SEX DISTRIBUTION IN CAD AND CVA PATIENTS

In this study it is observed that prevalence of CAD and CVA in a total of 100 cases is more common in males when compared to females.

This observation is supported by study of :

Orlando et al., [17]. He showed that prevalence of cardiovascular disease that includes both CAD and CVA is more common in males.

TABLE - 5

AGE SPECIFIC PREVALENCE OF METS IN CAD & CVA PATIENTS:

In this study it was observed that prevalence of metabolic syndrome is higher in elderly, almost 90% in the age group >70yrs when compared to 27% in 28-40 year age group.

This observation is supported by :

John E.Morely [27].

TABLE - 6.

SEX SPECIFIC PREVALENCE OF METS IN CAD & CVA PATIENTS:

As per this study, it is observed that metabolic syndrome incidence is higher in females 62%, when compared to males - 44%.

This study is supported by

Onan et al., 2002;

Azizi et al., 2003 [3],

Gupta et al., 2003 [18],

Ramachandran et al., 2003 [52].

TABLE – 7

PREVALENCE OF METS IN DIABETIC & NON DIABETIC

In this study, about 81% of diabetics had metabolic syndrome and 38% of non diabetics had metabolic syndrome so, prevalence of metabolic syndrome is higher in diabetics.

This observation is supported by :

Benghazi et al.,[5]

TABLE - 8

PREVALENCE OF METS IN HYPERTENSIVE AND NON - HYPERTENSIVES:

This study shows that metabolic syndrome is highly prevalent in hypertensives almost 73% when compared to 37% in non hypertensives.

This obsevation is supported by :

Kjeldsen & co., [31] in Journal of hypertension.

TABLE – 9

PREVALENCE OF METS IN SMOKERS:

In this study, among 100 patients, about 39 were smokers and 61 were non smokers. Metabolic syndrome was present in 51% of smokers. This is slightly higher than the prevalence in non smokers.

Ishizaka nobukazu[25] and his colleagues in their study has shown that both former and current smoking was associated with an increased incidence of metabolic syndrome.

Table 10 : METABOLIC SYNDROME IN ALCOHOLICS:

Among 100 patients in this study, 41 were alcoholics. Among them, 37 % had metabolic syndrome which is lower than in non alcoholic group.

Mathew S.Freiberg's[38] study shows that mild to moderate alcohol consumption is associated with lower prevalence of Mets with a favourable influence on lipids, waist circumference and fasting Insulin.

Table 11: METABOLIC SYNDROME IN CAD AND CVA PATIENTS:

Prevalence of metabolic syndrome was about 52 % in CAD patients and 46 % in stroke patients as per this study.

This inference is supported by;

Jyotimoy pol, et al.,

San diego[55] has shown that men with metabolic syndrome has 78% greater risk of stroke than those without the combination & for women the risk was more than double.

Table 12: PREVALENCE OF INDIVIDUAL RISK FACTORS IN METABOLIC SYNDROME:

Among the individual components of metabolic syndrome, it is observed in this study that the decreasing order of prevalence is Hypertension, dyslipidema, impaired fasting glucose and increased waist circumference in a total of 49 metabolic syndrome cases.

This observation is supported by

1. Naresh Trehan et al.,[45]
2. Reddy K.S. et al.,[53]
3. V. Achari et al.,[66]

CONCLUSION

- There is high prevalence of metabolic syndrome in CAD patients.
- There is high prevalence of metabolic syndrome in CVA patients.
- There is a strong association of central obesity with metabolic syndrome.
- There is a strong association of Dyslipidemia with metabolic syndrome.
- There is very strong association of Hypertension with metabolic syndrome.
- There is very strong association of Diabetes Mellitus with metabolic syndrome.
- There is a strong association of smoking with metabolic syndrome.
- There is decreased prevalence of metabolic syndrome among alcoholics.
- As age advances, prevalence of metabolic syndrome also increases.
- Females have increased prevalence of metabolic syndrome.

"LONGER IS THE WAIST LINE – SHORTER IS THE LIFE LINE"

So, "Cardiometabolic Risk Initiative" should be taken as national effort encouraging health care providers and general public to focus on the prevention,recognition and treatment of all risk factors of Metabolic syndrome.

By taking preventive measures,central obesity,Dyslipidemia,Hypertension and Diabetes Mellitus can be prevented and that will lead on to reduced occurrence of CAD and CVA.

PROFORMA

Prevalence of metabolic syndrome in coronary artery disease and cerebrovascular accident Patients at Thanjavur Medical College Hospital.

NAME : ADMITTING UNIT :

AGE : SEX : IP NO :

ADDRESS : DATE OF

ADMISSION :

OCCUPATION :

C/O,

1. CHESTPAIN : Yes / No
2. BREATHLESSNESS : Yes/ No
3. PALPITATIONS : Yes / No

(or)

1. INABILITY TO USE UPPER AND LOWER LIMB : Rt or Lt.

PAST HISTORY : DIABETES - Yes / No

HYPERTENSIVE - Yes / No

CAD/ CVA - Yes / No

HYPERLIPIDEMIA - Yes / No

SMOKING - Yes / No

ALCOHOL - Yes / No

FAMILY HISTORY :

PARENTS / SIBLING - Any H/O DM, HT, CAD, HYPERLIPIDEMIA

EXAMINATION :

1. PULSE RATE :
2. BLOOD PRESSURE :
3. EXAMINATION OF CVS :
4. EXAMINATION OF RS :
5. EXAMINATION OF CNS :

HEIGHT - METERS

WEIGHT - KGS

BMI -

WAIST CIRCUMFERENCE : - CM

HIP CIRCUMFERENCE : - CM

WC : HC : -

INVESTIGATIONS :

1. FASTING BLOOD SUGAR

2. SERUM LIPID PROFILE : TC

HDL

LDL

TGL

VLDL

TC: HDL

LDL: HDL

3. ECG

4. ECHO (or) CT BRAIN

WHETHER PATIENT COMES UNDER METABOLIC SYNDROME

ACCORDING TO ATP III GUIDELINES.

Yes/ No

ABBREVIATIONS

ACEI	-	Angiotensin Converting enzyme inhibitors
AHA	-	American Heart Association
ARB	-	Angiotensin II Type 1 receptor Blockers
ART	-	Antiretroviral therapy
AT1R	-	Angiotensin Type 1 Receptor
ATP	-	Adenosine Triphosphate
BMI	-	Body Mass Index
CAD	-	Coronary Artery disease
CKD	-	Chronic kidney discase
CRP	-	C- Reactive protein
CVA	-	Cerebrovascular Accident
CVD	-	Cardiovascular disease
DM	-	Diabetes mellitus
EGIR	-	European Group for the study of Insulin Resistance

ESRD	-	End StaGe Renal Disease.
ET-1	-	Endothelin 1
FFA	-	Free fatty acid
GCK	-	Glucokinase
GH-IGF	-	Growth Hormone - Insulin Like Growth Factor
HDL - C	-	High Density Lipoprotein Cholesterol
HIV	-	Human Immunodeficiency Virus
HNF	-	Hepatocyte Nuclear Factor
HTN	-	Hypertension
ICAM -1	-	Intercellular Adhesion Molecule - 1
IDF	-	International Diabetes Federation
IFG	-	Impaired Fasting Glucose
IGT	-	Impaired Glucose Tolerance
IL	-	Interleukin
IR	-	Insulin Resistance
LDL-C	-	Low Density Lipoprotein - Cholesterol
METS	-	Metabolic Syndrome
MODY	-	Maturity Onset Diabetes of Young

MRI	-	Magnetic Resonance Imaging

NCEP :

ATP III	-	National Cholesterol Education Programme : Adult Treatment- Panel III
NEFA	-	Non Esterified Fatty Acid
NF - Kβ	-	Nuclear Factor Kappa Beta
NHLBI	-	National Heart Lung and Blood Institute
NO	-	Nitricoxide
PAI -1	-	Plasminogen Activator Inhibitor - 1
PC	-	Prostacyclin
PCOD	-	Polycystic Ovarian Disease
PGI2	-	Prostaglandin I2.
PPAR	-	Peroxisome Proliferator - activated receptor.
RAAS	-	Renin - Angiotensin of Aldosterone System
SHBG	-	Sex Hormone Binding Globulin
S-LDL-C	-	Small, dense LDL-C.

SREBP	-	Sterol Regulatory Element Binding Proteins
TGL/TAG	-	Triglycerides / Triacylglycerol
TNFά	-	Tumour Necrosis Feator ά
TPA	-	Tissue Plasminogen Activator
WC	-	Waist Circumference
WHR	-	Waist Hip Ratio

REFERENCES

1. Amytis tolotiglin, MD, & Bruce ovbiagele, MD.Metabolic syndrome and Stroke.Neurology 2006:66:1344-49.

2. Andrewkates, Alan Zajarias and Anne Goldberg.Ischemic heart disease.

3. Azizi et al - Prevalence of metabolic syndrome in an Urban population; Tehran lipid and glucose study. Diabetes Res. Clin Pract ., 61 (1) 29-37.

4. Barroso, I., et al. Type 2 diabetes mellitus, Hypertension & Hyperlipidemia relation to reduced fetal growth. Diabet.Med.2005;22;517-35.

5. Benghazi - libya - A pilot study - libyan I med ACP : 080175. Metabolic syndrome in Type 2 Diabetes in Libya.

6. Cabauero , A.E., 2003 Endothelial dysfunction in obesity and Insulin resistance : a road to diabetes and Heart Cardiovascular disease trends in disease Obes. Res., 11, 1278-1289.

7. Chandran, M., Pnilips, S.A., Ciaraldi, T., Henry R.R.2003.Adiponectin;more than just another fat cell hormone.Diabetes care26(8),2442-50.

8. Current Criteria for clinical diagnosis of metabolic syndrome cleveland clinic journal of medicine, Vol 74, Number 3, Page 199-208, March - 2007.

9. Dr.V.Mohan, Premalatha- Prevalence of Metabolic syndrome in Urban South Indian Population. CURES study.

10. Dr.Pradeep G Tawalkar.Metabolic syndrome : Understanding the Defnition and Etiopathogenesis from Mets care time.

11. Earl S.Ford, Wayne H. Giles MD., MSC; William H.Dietz MD., Ph.D..Prevalence of metabolic syndrome in US Adults.JAMA 2002;287:356-59.

12. Ecker et al; The metabolic syndrome, Lancet 365; 1415, 2005.

13. Egeberg, 1962, Sugrue et al., 1985 Association between elerated F VIII & / or VWP level with atherosclerosis.Scand.J.Clin.Lab.Invest.,14,253-258.

14. Filipovsky., J., Ducimetiere., P., Eschwege, E., Richard, J.L., Rosselin, G., Claude, J.R.1996. The relationship of blood pressure with glucose, insulin, heart rate, free fatty acids and plasma cortisol levels according to degree of obesity in middle - aged men. J.Hypertense., 14 (2) 229-235.

15. Fuster V.ORowke RA, Walsh RA, Poole - Wilson P.Hunst's The Heart - Chap 91 - 'Metabolic syndrome, obesity and Diet'.

16. Gemamedina- Gomez, Christopher lelliott, and Antonio J.Vidal - Puig. Genetically modified mouse models of IR.

17. Giovanni orlandi, Andrea Gelli, Simona fanuchi, Gloria Tognoni, Giovanna Acerbi, Lenigi Murri. Prevalence of stroke and TIA in elderly.Stroke 2005;36;525-526.

18. Gupta A., Gupta, R., Sarna, M., Rastogi Prevalence of diabetes, impaired fasting glucose and IRS in an Urban Indian Population. Diabetes, Res Clin,Pract., 61. (1) 69-75.

19. Hales, C.N., Desai, and Barker, D.J.P.1992. Type 2 Diabetes mellitus : the thrifty phenotype hypothesis. Biochem.Soc.Trans.,24,341-350.

20. Hattersley. A.T., Tooke, J.E. 1999. The fetal insulin hypothesis : an alternative explanation of the association of low birth weight with diabetes and vascular disease. Lancet, 353, 1789-1792.

21. Heart and stroke statistical update - AHA stroke statistics In: 2001.

22. History of Metabolic syndrome' from Wikipedia, the free encyclopedia.

23. Hopkinson, Z.E., Sattar, N., Fleming, R., Greer, I.A., 1998. PCOS : the metabolic syndrome comes to gynaecology, BMJ, 317.329-332.

24. Ho,S.C.Chen, Y.M., Woo, J.L., Leung, S.S., Lam, T.H., Janus, E.D 2001. Association between simple anthropometric c indices and cardiovascular risk factor. Int .J. Obes . Relat Metab. Disord., 25 (11) - 1689 - 1697.

25. Ishizaka Nobukazu, Ishi Zaka Yuko, Toda Ei-Ichi, Hashimoto Hideki. Nagai Ryozo, Yamakado Minoru. Association between cigarette smoking, metabolic syndrome and carotid arteriosclerosis .Atherosclerosis ISSN2005,vol 181,381-385.

26. John K.Ninomiya, MSc., Gilbert L' Italien, Ph.d., Michael H.Criqui, MD., MPH; Joanna L.Whyte, MS., RD, MSPH; Anthony Gamst Ph.D, Ronald S. Association of metabolic syndrome with History of Myocardial Infarction and stroke in the Third National Health & Nutrition Examination survey.Circ.2004:109:42-46.

27. John E. Morley Aging and Metabolic syndrome.Neurobiology of Aging.vol 9,1988,9-16.

28. Juhan Vague et al., 1989b - NPHS; Meadle et al 1986 - Factor VII & Prothrombotic State. Lancet,1,1050-1054.

29. Kahn R.Buse J. Ferrannini E, et al., The metabolic syndrome : Time for a critical appraisal ; joint statement from ADA and European study of Diabetes.J.Hypertension.50(1);july 2006.

30. Katsuki, A.Sumida, Y.Muruashima, S., Fujii et al. Acute & chronic regulation of serum SHBG levels by plasma insulin concentrations in male Type 2 DM patients . J.Clin, Endocrinol metab., 81, 2515 - 19.

31. Kjeldson, suerre Ea; Naditch - Brule, Lisab, Pertini, stefanoc, Zidek, Walterd; fursang; esabll 'Inn erased prevalence of Mets in Uncontrolled Hypertension across Europe.

32. Kraija et.al., Age - Specific prevalence of Mets defined by IDF & NCEP-Norwegian HUNT 2 Study. Nutr,Metab(Lond)2005;2:2.

33. Laaksonen, D.E., Niskanen., L., Punnonen, K.Nyyssonen, K. Tuomainen, T.P., Valkonen, V.P., Salonen - Testosterone & Sex hormone - binding globulin predict the metabolic syndrome & diabetes in middle - aged men. Diabetes care,27(5),1036-1041.

34. Langley Evans, E.M., Van Pelt, R.E., Binder, E.F., Williams, D.B., Ehsani, A.A., Kohrt, W.M.2001. Intrauterine programming of hypertension by glucocorticoids. Life sci., 60 (15), 1213-1221.

35. Lowe at al., 1980; Zahavi et al., 1981.Increased platelet activation in Metabolic syndrome and Type 2 DM.

36. Marvin moser, James R.Sowers, MD., Henry R.Black, MD. Microalbuminuria,chronic renal disease and metabolic syndrome.

37. Marchesini, G., et al. 2003. Nonalcoholic fatty liver, steato hepatitis, and the metabolic syndrome. Am.J.Med,107(5),450-455.

38. Mathew S. Freiberg MD et al- 'Alcohol consumption and prevalence of metabolic syndrome in U.S. Diiabetes care:2054-2059,2004.

39. Mathews et al in 1985 -HOMA- from Wikipedia, the free encyclopedia.

40. MC Keigue P.M., Miller, G.J., Marmot, M.G.1989. CHD in south Asians overseas: a review. J.Clin.Epidemiol., 42, 597-609.

41. MC Keigue, P.M. 1992. CHD in Indians, Pakistanis and Bangladeshis : Actiology & Possibilities for prevention . Br.Hear J., 67, 341-342.

42. MC Keown, N.M., Meigs, J.B., Liu, S., Saltzman, E., Wilson, P.W.Jacques, P.F.2004. Carbohydrate nutrition, Insulin resistance and prevalence of metabolic syndrome in the Framingham offspring cohort. Diabetes care, 27 (2), 538-546.

43. Melissari M.Balbi. T.Gennar M.Olivetti.G. The aging of the heart : weight and structural changes in the left ventricle with age.GItal cardial 1991;

44. Miloo.M.Edwards,Mathew S.Maurer and RachelContemporary cardiology - Aging, heart disease and its management. Facts & Controversies.

45. Naresh Trehan - Escorts Heart Institute & Research centre Cardiovascular disease trends in India.

46. Natalia B. Volkova, Prakash C.Deedwania. Dyslipidemia in MetS.AJCD.7(4); 259-274, 2007.

47. Nesto, R.2004 C.Reactive Protein, Its role in inflammation, Type 2 Diabetes and cardiovascular disease, and the effects of insulin - sensitising treatment with thiazolidinediones. Diabet.M.,21(8),810-17.

48. Onat, A., Ceyhan, K., Basar, O., Erer, B.,Toprak, S., Sansoy, V.2002. Metabolic syndrome : Major impact on coronary risk in a population with low cholesterol levels - a prospective and cross sectional evaluation. Atherosclerosis, 165(2), 285-292.

49. Poehlman., E.T.Tchernof, A.1998. Traversing the menopause: Changes in energy expenditure and body composition Coron. Artery Dis., 9(12), 799-803.

50. Poulsen, P., Vaag, A., Kylik, K., Beek Nielson, H.2001. Genetic versus environmental aetiology of the metabolic syndrome among male and female twins. Diabetolgia 44 (5), 537-543.

51. R.Gupta,C.Deedwania - Prevalence of Metabolic syndrome in Indian Urban Population by International Journal of Cardiology - Volume 97, issue2, Page 257-261-

52. Ramachandran, A., Snehalatha, C.Sathyavani, K., Sivasankari, S., Vijay, V.2003. Metabolic syndrome in urban Asian Indian adults - a population study using modified ATP III criteria.

53. Reddy K.S., Cardiovasular disease on India.. World health state Q 1993 ; 46: 101-107. JAPI Vol - 52. Feb 2004.

54. Robert H.Eckel - Mechanisms of Components of Metabolic syndrome that predispose to diabetes and atherosclerotic CVD.

55. SANDIEGO - California - Metabolic syndrome double stroke risk - (CNN,Com).

56. Sarah.H.Wild,Christopher D Byre-The Global Burden of Metabolic syndrome and its consequences for diabetes and cardiovascular discase' by .

57. Savage et al., Human Metabolic syndrome resuling from dominant - negative mutations in nuclear receptor - gamma.Diabetes,52,910-917.

58. Scott M. Grundy MD., Ph.D., Chaur ; James I.Cleeman, MD., Co-Chair, stephen R. Daniels, MD, Ph.D., Karen A.Donato, MS, Robert H.Eckel MD et al. Diagnosis and management of MetS.jcem VOL.92,NO.2,399-404.

59. Song, Y., Niu, T., Manson, J.E., Kwiatkouski, D., Liu, S.2004. Are variants in CAPN 10 gene related to risk of type 2 diabetes? A quantitative assessment of population & family - based association studies. Am.J.Hum.Genet, 74, 208-222.

60. Sumita Dodani MD, MS from Department of Epidemiology, University of Pittsburgh 'Distribution and Determinants of Coronary Artery disease'.

61. Sung, R.Y., Tong, P.C., Yu., W.,Lau, P.W., Mok, G.T., Yam, M.C., Lam., P.K., Chan, J.C.2003. High prevalence of Insulin resistance and metabolic syndrome in overweight / obese preadolescent Hong Kong Chinese children aged 9-12 years. Diabetes care,26(1),250-251.

62. Tack.C.J., Ong, M.K., Lutterman, J.A., Smits, P.1998. Insulin induced vasodilatation & endothelial function in obesity/ Insulin resistance. Effects of Troglitazone. Diabetolgia,41(5),561-576.

63. University of Southampton - school of medicine - metabolic syndrome - global prevalence.

64. Venugopal, S.K., Devaraj, S.., Yuhanna, I., Shaul, P., Jialal, I.2002. Demonstration that CRP decreases eNOS expression and bioactivity in human aortic endothelial cells. Circulation, 106,1439.

65. Vernay,M.Balkau,B.,Moreau,J.G.Sigalas et al.,Alcohol consumption and IRS parameters.

66. V. Achari, AK Thakur. Association of major modifiable risk factors among patients with CAD- JAPI - Feb 2004. vol52,103.

67. Weedon, M.N., Gloyn, A.L., Frayling, T.M., Hattersley, A.T., Datey Smith, G., Ben-shlomo, Y.2003a. Quantitative traits associated with the Type 2 diabetes susceptibility allele on Kir 6.2.

68. Weiss, R., Dziura. J., Burgert., T.S., Tamborlane, W.V., Taksali, S.E., Yeckel, C.W., Allen, K., Hopes, Obesity and the metabolic syndrome in children and Adolescents NEJM 350 (23), 2362-2374.

69. Yarbrough, D.E., Barrett- Connor, E., Eritz- silverstein, D., Wingard., D.L. 1998. Birth weight, adult weight and girth as predictors of the metabolic syndrome in postmenopausal women: the Rancho Bernardo study.Diabetes care,21,1652-1658.

70. Younossi, Z.M., Diehl, A.M., Ong, J.P.2002. Non alcololic fatty liver disease: an agenda for clinical research. Hepatology 35 (4).

71. Zoratti, R., Godsland, , chaturvedi, N., Crook, D., Crook, D., Stevenson, J.C., et al. 2000. Relation of Plasma lipids to insulin resistance, NEFA and body fat in men from three ethnic groups: relevance to variation in risk of diabetes & coronary disease metab. Clin.Exp., 49, 245-252.

. No.	Name	IP No.	Age	Sex	K/C DM	K/C HT	Smoker	Alcohol	Family H/O	WC	BP	FBG	HDL	TGL	LDL	TC	ECG	CT Brain	Mets
1	Rajarathinam	986527	54	M	NO	NO	YES	YES	NO	98	140/90	104	27	187	126	152	WNL	Lt capsular infarct	YES
2	Paneerselvam	994715	55	M	NO	NO	NO	NO	NO	97	190/100	78	40	203	189	203	LVH	Lt capsular infarct	YES
3	Rasu	994665	63	M	NO	NO	NO	NO	NO	79	180/100	102	38	65	88	140	LVH	Lt MCA infarct	YES
4	Balakrishnan	996558	50	M	NO	NO	YES	YES	NO	77	120/80	110	47	156	84	165	WNL	Rt MCA infarct	NO
5	Mahalingam	992938	52	M	YES	YES	NO	NO	NO	96	140/90	104	29.7	108	61.7	172	WNL	Lt MCA infarct	YES
6	Appas	994698	60	M	NO	NO	YES	YES	NO	86	150/100	96	26	134	113	139	WNL	Rt MCA infarct	NO
7	Shanmugam	990982	75	M	NO	NO	YES	YES	NO	90	140/90	116	22	307	143	227	WNL	Rt MCA infarct	YES
8	Petchimuthu	991845	55	M	NO	YES	YES	YES	NO	72	180/100	96	34	185	109	181	WNL	Lt capsular infarct	YES
9	Saraswathi	986246	62	F	NO	NO	NO	YES	NO	82	120/80	86	39.8	90	102	160	WNL	Rt MCA infarct	NO
10	Mohammed Ali	1001306	65	M	NO	NO	YES	YES	NO	90	140/90	84	40	96	129	189	WNL	Rt MCA infarct	NO
11	Singaram	1002514	35	M	YES	YES	YES	YES	YES	96	160/100	132	48	232	64.6	196	WNL	Rt MCA infarct	YES
12	Karuppaiya	997464	54	M	NO	NO	YES	YES	NO	102	140/90	92	45	146	99.8	186	WNL	Rt MCA infarct	NO
13	Saravanan	997830	43	M	NO	NO	YES	NO	NO	95	170/100	95	52	140	128	208	WNL	Lt MCA infarct	NO
14	Krishnamoorthy	1001718	62	M	NO	NO	YES	YES	NO	86	180/100	60	46	88	198	192	WNL	Rt MCA infarct	NO
15	Kaliyaperumal	999044	66	M	NO	NO	YES	YES	NO	82	120/80	101	38	152	108	174	WNL	Rt MCA infarct	YES
16	Punniyamoorthy	997403	57	M	NO	YES	YES	YES	NO	77	130/80	78	58	131	129	214	WNL	Lt MCA infarct	NO
17	Mahendran	1000918	48	M	NO	NO	NO	NO	NO	80	190/100	96	47	158	128	187	LVH	Rt capsularinfarct	NO
18	Veerammal	999779	69	F	YES	YES	NO	NO	YES	110	180/100	188	52	168	121	207	LVH	Lt MCA infarct	YES
19	Kamatchi	990993	55	F	NO	YES	NO	NO	NO	86	150/90	88	45	99	115	180	WNL	Rt MCA infarct	YES
20	Chellammal	987263	72	F	NO	YES	NO	NO	NO	72	150/90	96	47	156	90	167	WNL	Lt MCA infarct	YES
21	Vairakannu	1003415	50	F	YES	YES	NO	NO	YES	70	160/100	150	52	152	141.4	240	WNL	Lt MCA infarct	YES
22	Ramavalli	998251	60	F	NO	NO	NO	NO	NO	72	130/90	75	39	128	95.4	260	WNL	Rt capsularinfarct	NO
23	Manimekalai	975733	37	F	NO	NO	NO	NO	NO	82	120/80	116	40	156	77.8	147	WNL	Rt MCA infarct	YES
24	Vishalatchi	977750	85	F	NO	YES	NO	NO	NO	62	160/80	96	42	153	72.6	140	WNL	Lt MCA infarct	YES
25	Dhanraj	1003434	28	F	NO	NO	YES	YES	NO	60	120/80	74	39	158	83.4	154	WNL	Lt MCA infarct	NO

. No.	Name	IP No.	Age	Sex	K/C DM	K/C HT	Smoker	Alcohol	Family H/O	WC	BP	FBG	HDL	TGL	LDL	TC	ECG	CT Brain	Mets
26	Selvaraj	986185	66	M	YES	YES	YES	NO	YES	60	150/86	174	58	180	103	187	WNL	Rt MCA infarct	YES
27	Pitchai	986259	61	M	NO	NO	YES	YES	YES	76	160/100	78	36	166	166	216	LVH	Rt capsularinfarct	YES
28	Ganesh	994809	49	M	NO	YES	YES	YES	NO	84	180/100	84	42	79	133	191	WNL	Rt MCA infarct	NO
29	Uthirapathi	991843	35	M	NO	NO	NO	YES	NO	80	120/80	92	49	132	98	174	WNL	Lt MCA infarct	NO
30	Paranthaman	987634	43	M	NO	NO	YES	YES	NO	93	140/90	104	49	109	127	198	WNL	Rt MCA infarct	YES
31	Thangaiyan	990527	52	M	NO	NO	YES	YES	NO	86	120/80	126	48	152	64	159	WNL	Rt MCA infarct	NO
32	Thangaiyan	986285	62	M	NO	NO	NO	NO	YES	86	130/80	88	40	152	72	180	WNL	Lt capsular infarct	NO
33	Thirunavukarasu	986205	49	M	NO	NO	YES	YES	NO	80	120/80	104	44	132	89	172	WNL	Lt MCA infarct	NO
34	Ramaiyan	986275	60	M	YES	NO	YES	NO	NO	80	150/90	119	38	166	104	202	WNL	Lt capsular infarct	YES
35	Rajangam	1002650	64	M	YES	NO	NO	NO	YES	72	120/80	124	42	144	106	184	WNL	Lt MCA infarct	NO
36	Sivasami	997415	57	M	NO	NO	NO	NO	NO	82	130/80	80	49	146	96	172	WNL	Lt MCA infarct	NO
37	Vellakannu	999955	53	M	NO	NO	NO	NO	NO	76	140/90	78	52	172	132	190	WNL	Lt MCA infarct	NO
38	Sekar	994813	46	M	YES	NO	NO	YES	YES	82	140/80	102	41	146	105	196	WNL	Rt MCA infarct	NO
39	Chinnaponnu	9001346	55	F	NO	NO	NO	NO	NO	82	120/80	116	46	142	104	184	WNL	Rt MCA infarct	NO
40	Kathirmani	978302	65	F	YES	YES	NO	NO	NO	92	150/96	144	39	186	112	186	WNL	Rt MCA infarct	YES
41	Saraswathi	999152	52	F	NO	NO	NO	NO	YES	86	130/80	78	39	146	104	186	WNL	Lt MCA infarct	NO
42	Shanmugavadivu	971695	60	F	NO	YES	NO	NO	YES	88	150/90	96	38	158	126	204	WNL	Rt capsularinfarct	YES
43	Lakhsmi	967792	62	F	NO	NO	NO	NO	NO	86	120/80	98	36	146	101	176	WNL	Rt MCA infarct	NO
44	Amirtham	984279	59	F	YES	NO	NO	NO	NO	88	150/90	132	38	166	135	206	LVH	Rt MCA infarct	YES
45	Alamelu	980551	65	F	NO	YES	NO	NO	NO	76	140/100	86	39	142	104	168	WNL	Lt MCA infarct	NO
46	Alagammal	980346	65	F	NO	NO	NO	NO	NO	82	120/80	82	39	146	107	182	WNL	Lt MCA infarct	NO
47	Vairam	991848	60	M	NO	NO	YES	YES	YES	88	160/90	116	38	162	130	182	WNL	Rt MCA infarct	YES
48	Durai	990054	48	M	NO	NO	YES	YES	YES	82	140/90	92	37	136	104	160	WNL	Lt MCA infarct	NO
49	Palanisamy	989935	52	M	NO	NO	NO	NO	NO	86	130/80	90	40	142	112	175	WNL	Lt MCA infarct	NO
50	Narayanan	986609	62	M	YES	YES	YES	YES	YES	92	150/96	126	34	176	142	216	WNL	Rt MCA infarct	YES

K/C - known case of

WC - Waist Circumference

WNL - Within Normal Limits, LVH - Left Ventricular Hypertrophy

S. NO	NAME	IP NO	AGE	SEX	k/c DM	k/c HT	Smoker	Alcohol	Family history	WC	BP	FBG	HDL	TGL	LDL	TC	ECG	ECHO	MetS
1	Purushothaman	996520	76	M	NO	YES	YES	YES	YES	105	160/100	104	34	196	154	204	IWMI	CAHD	YES
2	Prakasam	996545	55	M	YES	NO	YES	NO	NO	99	140/90	138	38	162	112	195	IWMI	CAHD	YES
3	Panditham	970932	65	F	YES	YES	NO	NO	NO	96	190/100	106	45	197	122	207	IWMI	CAHD	YES
4	Rajalakshmi	977739	52	F	NO	YES	NO	NO	NO	96	160/100	90	37.9	177	156	230	ASMI	CAHD	YES
5	Govindaraj	990071	52	M	NO	YES	YES	YES	NO	92	140/100	92	31	149	90	151	ASMI	CAHD	YES
6	Kauveri	982142	56	F	YES	YES	NO	NO	YES	80	160/100	122	35	186	110	182	IWMI+PWMI	CAHD	YES
7	Anandhan	986215	30	M	NO	NO	YES	YES	NO	98	110/70	76	38.6	52	104	153	IWMI	CAHD	NO
8	Sahaya doss	986250	39	M	NO	NO	NO	NO	NO	90	150/100	92	33	251	187	271	IWMI+PWMI	CAHD	YES
9	Ponnusamy	996060	62	M	YES	YES	YES	YES	YES	86	140/80	212	36	115	90	149	Ext.AWMI	CAHD	YES
10	Ramaiyan	996865	52	M	NO	NO	NO	NO	NO	86	140/100	86	39	146	102	163	IWMI	CAHD	NO
11	Jeyamary	967875	56	F	NO	NO	NO	NO	NO	90	160/100	160	38	156	134	196	AWMI	CAHD	YES
12	Sivanesan	990516	49	M	NO	NO	NO	YES	NO	79	110/70	86	33.6	49	152.6	196	ASMI	CAHD	NO
13	Muniyandi	988072	67	M	NO	NO	NO	NO	NO	89	110/70	96	31.6	82	99	148	AWMI	CAHD	NO
14	Palanivelu	986721	57	M	YES	YES	YES	NO	YES	87	140/90	121	35	173	140	202	AWMI	CAHD	YES
15	Veeraiyan	989953	44	M	NO	NO	YES	YES	YES	70	110/70	96	48	180	155	199	ASMI	CAHD	NO
16	Paneerselvam	998335	55	M	YES	NO	YES	NO	NO	88	110/70	186	41	84	133	191	Ext.AWMI	CAHD	NO
17	Abdul majith	1000765	67	M	YES	YES	YES	YES	YES	86	140/80	242	38	176	140	220	IWMI+PWMI	CAHD	YES
18	Paramasivam	1004399	55	M	NO	NO	NO	NO	NO	88	140/100	84	52	67	133	199	IWMI	CAHD	NO
19	Ekambaram	1000907	61	M	NO	NO	NO	NO	NO	94	160/100	102	36	75	83	134	ILMI	CAHD	YES
20	Arokiya joseph	1005180	34	M	NO	NO	NO	YES	NO	86	160/100	75	46	130	88	160	ASMI	CAHD	NO
21	Ramaiyan	998451	71	M	YES	NO	NO	NO	NO	92	110/80	120	38	156	96	175	ASMI	CAHD	YES
22	Chinnasamy	996548	72	M	NO	NO	YES	YES	NO	70	100/60	102	57	102	150	227	IPWMI+RVMI	CAHD	NO
23	Ganesan	1000456	56	M	NO	NO	YES	YES	NO	93	120/70	105	44	85	93	153	IWMI	CAHD	NO
24	Kaliyaperumal	997469	73	M	YES	NO	NO	NO	NO	104	170/100	120	48	88	101	167	ASMI	CAHD	YES
25	Samsudeen	990022	63	M	NO	NO	YES	YES	NO	84	140/90	120	45	92	106.6	170	Ext.AWMI	CAHD	NO
26	Dhanalakshmi	974211	55	F	NO	NO	NO	NO	NO	82	180/110	90	48	86	106.8	174	AWMI	CAHD	YES
27	Velammal	970129	50	F	NO	NO	NO	NO	NO	72	160/100	75	41	110	124	167	ASMI	CAHD	NO

S. NO	NAME	IP NO	AGE	SEX	k/c DM	k/c HT	Smoker	Alcohol	Family history	WC	BP	FBG	HDL	TGL	LDL	TC	ECG	ECHO	MetS
28	Barsha beevi	970953	46	F	YES	YES	NO	NO	YES	73	140/100	165	41	195	174	254	HLMI	CAHD	YES
29	Mariammal	970128	72	F	NO	NO	NO	NO	NO	82	140/90	96	46	156	104	200	AWMI	CAHD	YES
30	Selvaraj	999149	41	M	NO	NO	NO	NO	NO	82	120/70	98	43	102	83.6	147	IWMI	CAHD	NO
31	Natarajan	1000010	55	M	NO	YES	NO	NO	NO	66	130/86	185	36	155	104.4	154	IWMI+PWMI	CAHD	YES
32	Prakash	1000920	49	M	YES	YES	NO	NO	YES	80	170/100	102	38	88	94	160	IWMI	CAHD	YES
33	Devendran	999982	46	M	NO	YES	NO	NO	NO	76	140/100	96	34	105	91.6	147	IWMI	CAHD	NO
34	AbdulRahim	998281	75	M	YES	NO	NO	NO	NO	90	150/90	126	51	122	100.6	167	IWMI	CAHD	YES
35	Rajendran	1004411	40	M	NO	YES	YES	YES	NO	100	140/90	96	54	97	47.4	174	ALMI	CAHD	NO
36	Velu	1003423	55	M	NO	NO	YES	YES	NO	70	110/70	94	46	198	104	133	ALMI	CAHD	NO
37	Pitchai	985177	58	M	NO	NO	YES	YES	YES	104	140/90	96	38	119	45	166	IWMI	CAHD	YES
38	Maniraj	986309	63	M	NO	NO	YES	YES	NO	77	180/100	168	48	110	92.24	115	IWMI	CAHD	NO
39	Thathuvamary	973883	75	F	NO	YES	NO	NO	NO	60	180/110	94	48	129	126	166	ASMI	CAHD	NO
40	Ramani	978760	55	F	YES	YES	NO	NO	YES	67	170/90	200	42	165	97.2	196	IWMI+PWMI	CAHD	YES
41	Subramani	989939	65	M	NO	YES	NO	NO	NO	103	140/80	96	32	94	157	128	Ext.AWMI	CAHD	YES
42	Veeramalai	987141	60	M	NO	NO	NO	NO	NO	85	160/70	72	41	93	85	217	ASMI	CAHD	NO
43	Chinnadurai	988991	55	M	NO	NO	YES	YES	NO	70	180/110	106	30	98	61	135	IWMI+PWMI	CAHD	YES
44	Anthonimuthu	995778	43	M	NO	NO	YES	YES	NO	82	120/80	92	56	112	124	140	IWMI	CAHD	NO
45	Nijam	1000885	35	M	NO	NO	NO	YES	NO	82	120/70	95	36	186	133	198	IWMI	CAHD	NO
46	Thangaponnu	975768	72	F	NO	YES	NO	NO	NO	88	140/90	84	34	182	89	204	AWMI	CAHD	YES
47	Chandra	970901	58	F	YES	NO	NO	NO	NO	76	120/80	132	38	146	133	196	AWMI	CAHD	NO
48	Nagarathinam	974785	62	F	YES	NO	NO	NO	YES	74	130/80	112	50	162	116	202	ASMI	CAHD	NO
49	Naheswari	967049	52	F	NO	NO	NO	NO	NO	78	120/80	96	36	140	124	198	IWMI	CAHD	NO
50	Padmavathy	970038	70	F	NO	YES	NO	NO	NO	88	140/90	84	34	172	133	204	AWMI	CAHD	YES